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Vol. II. No. 2. Serial No. 6 *April-June, 1918*

ENDOCRINOLOGY:

The BULLETIN of the ASSOCIATION for the STUDY of INTERNAL SECRETIONS.

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ENDOCRINOLOGY:

The BULLETIN of the ASSOCIATION for the STUDY of INTERNAL SECRETIONS

APRIL—JUNE, 1918

THE THYROID HORMONE AND ITS RELATION TO THE OTHER DUCTLESS GLANDS*

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Much of the research work concerning the ductless glands has been from the viewpoint of relating some one gland to some particular portion or restricted function of the body. Thus, the pituitary has been associated with the growth of the bones and certain skeletal formations, the thyroid has been associated with the nerves, and some writers have satisfied themselves that the activity of certain ductless glands is explained by clinical syndromes wherein only portions of the body show abnormalities. There have been relations suggested which were based on embryologic grounds. Organs and tissues derived from some common source have been supposed to be more or less related in function. Some of the most elaborate relationships of the ductless glands are based on histologic findings. The vast

*Presented before the meeting of the Association for the Study of Internal Secretions, June, 1918, Chicago.

amount of research work that has been done with this object in view has indeed told us a great deal concerning the relationships of the ductless glands to certain bodily functions, but beyond this knowledge one cannot penetrate without new tools, and without applying quantitative determinations to the physiologic processes involved.

Before the chemical balance came into existence, the alchemist held sway over the theories of matter and the relationships existing between chemical substances. The phlogiston theory was unassailable on any ground other than quantitative analysis. From a survey of the literature today concerning the ductless glands we cannot boast of being very far out of the alchemist's age, and as yet very few investigators have approached the subject in a quantitative manner, with a realization of the actual problems existing.

For a complete analysis of the exact chemical reactions produced by this or that gland, nothing short of the actual isolation of the products in question can really solve the problem, and even after the chemical substances responsible for the activity of the various glands have been isolated, the interpretation of their physiologic functions requires, not only the microscope, the kymograph and the chemical laboratory, but most of all the application of physics, chemistry, hydrolics and mechanics. Too much emphasis has been laid in the past on clinical and experimental conditions that are only partial expressions of a fundamental reaction which in almost every case has so far escaped detection. In the meantime these minor details have been stretched

to the utmost in order that they may fit the theory of the supposed function of the gland in question.

Realizing that the function of the thyroid must be based on simple chemical reactions, and trusting in the probability that the substance producing these reactions would be stable enough to be separated, the isolation of the iodin compound occurring in the thyroid was begun by me eight years ago. During this investigation a very large amount of fresh thyroid glands has been used, and the work has been pushed in several directions so that now not only has the isolation of the substance been accomplished but it has been analyzed, its empirical and structural formulae have been determined, and its synthesis has been completed.* The physiologic action has been studied, and a large number of patients have been treated in the Clinic.

All this work has emphasized the necessity of viewing the function of any endocrine gland on the very broadest possible grounds. For example, in cretinism there is a certain characteristic expression of the face, the long bones do not grow normally, the skin is dry and scaly, the hair is scant and brittle, there is no ambition, and mental activity is very much below normal. Shall one then say that the thyroid controls the length of the long bones, the skin, the hair and the nerves? This is all true, but it does not deal with the actual function of the gland and the chemical processes involved. It is following only so far as the eye can see. In this instance quantitative studies have been directed to anatomic changes and not to physiologic processes. A change

*Mr. Osterberg, working in our laboratory, succeeded in synthesizing a small amount of thyroxin in December, 1917. Further work is in progress.

in the physiologic function is being interpreted in terms of the end result produced by the change. One almost loses sight of the fact that the thyroid is just as vitally concerned in normal conditions. To the majority of those most interested the function of the thyroid does not mean a physiologic process based on chemical reactions, but the word brings to mind a disturbance defined in clinical terms.

According to the older view the active consituent of the thyroid functions within the gland itself. The blood passing through the gland is purified; before it enters the gland it is toxic to the organism, and after leaving the gland it is not toxic. Others have held that the location of the activity of the substance was in and through the nervous system, that through the nerves the various thyroid manifestations were brought about and that the secretion was carried from the gland to the nerves by the blood stream.

During the past ten years Plummer has been making a very detailed study of the function of the thyroid, and he has been led to believe that the location of the active constituent of the thyroid, when it functions, is within the cells not of any particular set of organs or portion of the body, but that it is a constituent of cellular life and activity. Plummer states that the active constituent of the thyroid determines the rate at which any particular cell can produce energy, that is, it establishes the quantum of energy which any cell can produce when it is stimulated either from within itself or from without, so that the thyroid is directly related to the production of energy within the body. He has shown that one-third of one milligram of the active constituent of the thyroid increases the basal metabolic

rate one per cent in an adult weighing approximately 150 pounds. Here we have not only a definition of the function of the thyroid, but it is expressed in mathematical terms with such exactness that the number of milligrams of the substance functioning within the entire body can be estimated. It is between 23 and 50 milligrams, that is, between one-third and two-thirds of one grain.

We are still confronted with the problem of the exact chemical reactions involved, but here again a great deal of light is thrown on the problem by the chemical constitution of the active constituent of the thyroid. For reasons given hereinafter the substance has been named "Thyroxin."

When thyroxin is given to a myxedematous patient all the symtoms due to myxedema are promptly relieved. When it is given in too large amounts hyperthyroid symptoms are produced. This has been known now for more than three years, and on these grounds it has been stated that thyroxin is the active constituent of the thyroid. But the fact that a physiologic response is produced by the administration of a substance is not an explanation of the physiologic function of that substance, and it was not until a quantitative value was placed on thyroxin that the real physiologic processes involved could be demonstrated. It seems that one of the most important results of this work has been the furnishing of the material with which quantitative values could be determined.

The moment we know that in a myxedematous patient the administration of 10 mg. of thyroxin increases the basal metabolic rate 30 per cent, we have the key to the explanation of the relief of a very com-

plex clinical syndrome. The edema is relieved. The sluggish mentality is relieved. The dry scaly skin becomes moist. The hair ceases to fall out and becomes soft. The voice that has been very slow, returns to its normal tone and character. The mentality which has been befogged becomes clear, and the individual expresses his normal personality. In short, every cell in the body responds with its own expression of activity. It seems impossible that all this can be done with a single crystalline substance, and because our knowledge has been limited as to just what and how much was going on, we have let visible changes lead away into theories that are narrow and which obscure rather than enlighten. But, when we know that simultaneously with the clinical improvement the basal metabolic rate has been increased 30 per cent, it follows axiomatically, from laws of mechanics, hydrolics and physics, that very fundamental changes have occurred throughout the entire body. It has long been known that the thyroid influences basal metabolic rate in the body. It is a present-day conception that it is through metabolic processes that the thyroid produces its physiologic effect, but the scope of this action and the chemical processes involved have not been emphasized or established.

In order to explain the action of thyroxin, when 10 milligrams of the substance increases the metabolic rate 30 per cent, as Plummer puts it, it would take a discussion as broad as biology itself. This aspect of the question must receive greater attention in order to bring out the physiologic processes involved in the function of the thyroid, and with it, the other ductless glands. The scope of the problem

is so broad that several investigators viewing it from entirely different standpoints can each obtain results satisfactorily conforming to their conclusions, but no one of which forms a fundamental physiologic process. For instance, investigating the question of resistance to infection, the removal of the thyroid establishes the fact that in thyroidless animals infection is much more prevalent. This is of interest to the bacteriologist, serologist, immunologist, etc. The fact that the growth of bones is retarded is an entirely different phase of the subject, and so, a long list of investigations concerning the thyroid which have been carried on with positive results leading to various conclusions concerning its activity, could be cited.

Until it was shown that the confusing clinical syndrome found in myxedema could be entirely relieved by a single substance, the problem as to how many active constituents occurred in the thyroid could not be settled. In fact, the fundamental reaction underlying all expressions of thyroid activity could not be made as long as clinical symptoms alone were used as a criterion of physiologic activity. But, establishing the relation of thyroxin to the basal rate of metabolism in mathematical exactness furnishes the first clew to the physiologic processes involved, and it is evident that physiologic response to an injection of thyroxin is found in a summation of the activity of all the cells in the body. If anyone chooses to investigate any one particular process he will find that process altered, for a change in metabolic rate is accompanied by fundamental changes in every aspect of the reactions going on within the body. This is where the application of physics, mechanics,

hydrolics and chemistry must be made in order to understand, not only the changes produced by the administration of thyroxin, but what the effect of a second factor would be.

The injection of adrenalin into an animal with a normal basal metabolic rate will necessarily be different from the injection of adrenalin into an animal with a metabolic rate 30 per cent above normal, if viewed purely from a consideration of the physics involved. As Plummer has pointed out, it is possible to explain the supposed relation between thyroid and adrenalin on grounds involving the rate of flow of the blood, entirely apart from any other action.

When it comes to establishing relations between the other ductless glands and the thyroid, progress can only be made when the various activities of the glands are viewed in as broad an aspect as Plummer has suggested for the action of thyroxin. Disturbances of the pituitary lead to changes in basal metabolic rate which are marked but are less than those found in thyroid disturbances. Changes in the pancreas and what we know of the adrenal also lead to changes which are smaller than that produced by thyroxin. We can at least tentatively assign to the thyroid the supplying of an agent which is of fundamental importance in the production of energy. This can be carried one step further in a chemical sense, and we may assume that thyroxin is involved in the production of carbon dioxide. The other ductless glands then assume positions of secondary importance to the thyroid, in carrying out these chemical reactions, and may be assigned the role of preparing the various metabolites for their final action with

thyroxin. No definite hypothesis can at this time be given beyond the fact that the various clinical syndromes produced by hyper- or hypo-action of the various glands, are syndromes resulting from the effects of these substances throughout all the cells of the body, through their action in maintaining the rate of energy production going on within the cells.

It is perfectly possible to explain the apparent selective action of various internal secretions to restricted portion of the body on these grounds, and in fact selective action vanishes when the action of the gland is placed on this broader basis.

Beside the action suggested for certain of the ductless glands of preparing metabolites for their final interaction with thyroxin with the production of energy, we must also assign to some agents within the body the task of taking care of bi-products and of elaborating other substances. Nitrogen compounds include toxic substances among their number. For the proper elaboration of these compounds, which assume fundamental importance in normal physiology, some very substantial mechanism must exist. That certain of the ductless glands should be given the power to affect the rate at which the body can prepare and care for nitrogenous compounds seems highly probable, and of late the parathyroid assumes great importance as one of the glands thus involved. That others of the glands are also concerned also seems to be indicated.

It was therefore of great interest to determine the chemical nature of this iodin containing compound which occurs in the thyroid and is so fundamentally involved in normal physiology. Analysis has shown that it contains an indol group with the

iodins undoubtedly attached to the benzene ring, and that on the carbon atom adjacent to the imino group of the indol ring there is an oxygen atom. (Fig. 1.)

Figure 1

The structural formula of the active constituent of the thyroid.

For reasons given hereinafter, it appeared desirable to emphasize the presence of the oxy-indol nucleus and it appeared equally desirable not to emphasize the presence of iodin. The substance was therefore named "Thyro-oxy-indol," which has been shortened to "thyroxin" for every-day reference to the substance. At first we attempted to show that the activity of thyroxin was due to the oxygen condensing with the amino group of an amino acid and the carboxyl group of the amino acid reacting with the imino group of thyroxin. It has been shown, however, that this does not occur; but that the physiologic activity of the substance is produced by the CO-NH groups has been demonstrated as follows:

The injection of pure thyroxin is followed by a very definite and marked physiologic response. When the hydrogen on the imino has been replaced with acetyl the substance loses its physiologic activity and the injection of the substance is without demonstrable effect. Investigation of the acetyl showed that, in alkaline solution, the indol form of the compound no longer exists, but that there is hydrolysis of the CO and NH groups resulting in the opening of the ring and the formation of COOH and NH_2 (Fig. 2). Further investigation showed

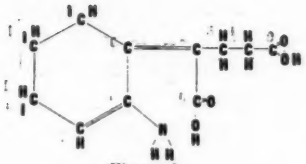

Figure 2

The open ring form of thyroxin as it exists in the body.

that thyroxin behaves in this same way, and that it exists within the body, not in the closed ring form such as is present in indol, but in the form COOH NH_2. The ability of the indol ring to thus open, furnishes the first concrete conception of how the substance behaves chemically within the body. The fact that both thyroxin and the acetyl derivative exists in open form, suggests that the reason for the inactivity of the acetyl is because of interference with the chemical reaction associated with the NH_2 group of thyroxin. One is at once struck with the fact that the open and closed forms of thyroxin bear to each other the same relation as does creatin to creatinin, and that the same relation exists between amino acids and the form in which amino acids are united in protein. Establishing these active groups emphasizes the importance of the chemical nucleus CO NH and COOH NH_2 within the body, which appears to be a necessary structure for the carrying out of chemical changes leading to the production of energy.

Patients with complete atrophy of the thyroid have basal metabolic rates approximately 40 per cent below normal. It has been shown that administration of thyroxin alone can bring back and maintain the normal metabolic rate in such patients. But in complete atrophy of the thyroid, the complete or

nearly complete absence of thyroxin may be assumed. The question arises as to what maintains energy output from 100 per cent below normal, which would be death, up to 40 per cent below normal, the point to which basal metabolism sinks in the absence of thyroxin. May it not be the other chemical substances in the body possessing the same grouping that occurs in thyroxin? These are amino acids and proteins, creatin and creatinin, and a few other less well-known compounds. It seems probable that on the administration of thyroxin a reaction which has been carried on within the body by other compounds is merely increased in rate, but that there is no difference or disturbance of the reactions that have been going on.

In regard to the relation of iodin to the activity of thyroxin, the presence of iodin in the compound must exert some influence, and it seems not improbable that the presence of iodin renders the active groups more reactive. In the absence of iodin it would take a greater working pressure to bring about its reaction. The substitution of the iodin by hydrogen or chlorine or bromine would undoubtedly be followed by an alteration in the degree of reactivity of the substance, but its gross chemical nature and properties would not be altered thereby. That the iodin breaks off from the molecule and is used as iodin per se for any purpose, seems absolutely impossible because Plummer has shown that this substance functions for as long as from 15 to 21 days after being administered, and that it acts as a true catalyst, being used over and over, hour after hour, without destruction except at a very low rate. It is finally removed from the body either by actual de-

struction, or by slow loss in an undestroyed form. Our knowledge of other catalytic agents shows that poisoning of catalysts is common if not universal, so that its slow destruction is to be expected.

The exact chemical reactions involved when this substance functions are still unknown, but that the substance possesses the formula as shown above is established by the ultimate chemical analysis of its derivatives. That the active groups present in thyroxin are a necessary mechanism for the production of energy within the body seems highly probable, and it is of great interest and significance that there exists a close analogy between this substance, whose exact effect on metabolism we know, and other substances, creatin, creatinin, amino acids and proteins, which are also intimately associated with reactions occurring within the animal organism. Are these substances also concerned in the maintenance of the basal metabolic rate?

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THE PITUITARY BODY AND POLYURIA

B. A. Houssay, Buenos Aires

The following article comprises a summary of various of our observations previously published or reported before the Asociación Médica Argentina (May 3, 1915) and abstracted in La Prensa Médica (1915, p. 451). A concluding report of the entire investigation is shortly to appear.

Different immediate effects occur when pituitary extracts are administered to dogs intravenuously. The chemical composition of the gland is very constant, as are the physiological effects of the gland extracts, but these effects vary qualitatively according to the methods of preparation. Extracts of the fresh glands produce brief vasodepression followed by augmented arterial pressure; during the depressor phase of the reaction the kidney volume is diminished and oliguria occurs, but when the pressure rises a renodilation accompanied by more or less marked diuresis is noted. Sometimes we have noted an initial renocontraction with or without general hypotension which persists for a short time into the hypertensive phase; this may or may not be followed by renodilatation. In other instances, in case of the more strongly hypertensive extracts, kidney dilation and diuresis, together with augmented blood pressure, occur as the primary reaction without initial hypotension. This effect is observed generally in case of extracts prepared by the aid of metalic salts, of decoctions of powder of the posterior lobe desiccated at 37-45° and of preparations from glands extracted with alcohol. It would appear, then, that there occur in pituitary

extracts both renocontractor and renodilator substances, one or the other predominating according to circumstances. The diuretic effects run parallel with the renovascular effects.

When we observe the diuresis of twenty-four hours, the effects are not the same and they vary according to the animals. In rabbits there is constantly noted a strong oliguria, but in dogs and in the human beings the effects are extremely variable, and sometimes can be contradictory. In man it is common to observe diuresis, especially in oliguries, although this action is less than in case of other diuretic substances. In polyuric men the effect is almost constantly a depression of urine secretion. In the rabbits a tolerance to the drug develops and the initial diuresis returns at the end of a few weeks, in spite of daily injections.

We conclude from the pharmacologic action of pituitary extract that it is not permissible to deduce an insufficiency of the pituitary body from the successful use of the extracts in polyuria.

We cannot agree that the cerebro-spinal fluid has, as Cushing has claimed, the same effects as pituitary extracts. We have demonstrated, with Giusti in 1911, that the latter retains its actions, in spite of being treated with subacetate of lead, while in case of former the action is lost. In 1913 we proved, as Mackenzie has proved (Quart. Jour. Exp. Physiol., 1911, p. 305), that the cerebro-spinal fluid had not the diuretic action and not even the galactogogue action, which are the most specific tests of pituitary material. For this reason we cannot concur in the opinion that the active components of pituitary extracts pass to the cerebro-spinal fluid. This does

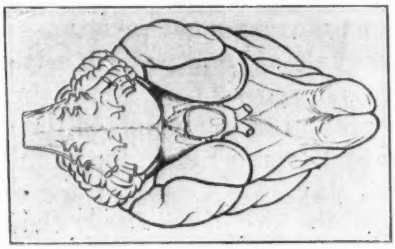
not signify that we deny that the pituitary body has some secretions that pour into the third ventricle (as Hering affirms), but it is not proved that it is the diuretic or hypertensive substance.

The operations made for the removal of the pituitary gland produce different results in adult dogs and in puppies. In the adults it is very often oliguria, while in puppies it is polyuria that occurs during the first few succeeding days. These results are in agreement with those of Cushing and his co-workers. These effects are due merely to the trauma, and it is possible to observe them in animals operated upon without actually removing the gland, or even touching it. The intervention of the pituitary in the polyuria can be excluded, because we have obtained this reaction in cases in which we have removed the whole gland, proved by a series of sections of this region, studied histologically.

As we were not able to study directly the injuries of the cerebral basal zone, because the operation to disclose it produced oliguria (adult dogs) or polyuria (puppies), we employed a method similar to that of Camus and Roussy (Presse Médicale, 1914, p. 517). Pricking through the sphenoid with a hot needle or utilizing iron filings (in which manner it is possible to observe the dogs a very long time, while with the pricking it is necessary to kill them a few days after the puncture because the injury disappears quickly), we obtained in all cases identical results. If the pricking had been in a determined cerebral zone we observed polyuria, and if the pricking had been outside of this zone the polyuria did not occur. In one case the puncture encountered the pituitary stalk

and penetrated into the third ventricle, without injuring the brain and no polyuria developed.

The zone able to generate polyuria in our experiments was limited behind, by the peduncle protuberance; before, by a line near the anterior limit of the optic chiasma and laterally, as shown in the accompanying drawing.



Ventral surface of brain of dog showing zone injury of which produces changes in kidney secretion. Zone outlined by dash line.

Finally, we consider that the cerebral basal zone can generate polyuria. We do not deem it probable that the pituitary constitutes a part of this zone, although it is possible that the posterior lobe of the gland participates.

It cannot be accepted, now, that polyuria is due to a diuretic hypersecretion of the pituitary gland.

ON THE SEASONAL VARIATION IN THE IODINE CONTENT OF THE THYROID GLAND.

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In previous communications on this subject it was shown that a marked seasonal variation exists in the iodine content of the thyroid gland of cattle, hogs and sheep. There is in general from two to three times as much iodine present in the glands in the months between June and November as in the months between December and May. (1) A more or less regular seasonal change in the size of the fresh gland exists in the case of cattle and sheep, but not in hogs. A consideration of the several causes for the fluctuations leads to the conclusion that the temperature is perhaps the most important of all. (2)

These investigations were conducted from September, 1911, to December, 1913, during which time samples of fresh glands were collected twice a week and stored at freezing temperature. The glands were trimmed, prepared and analyzed twice a week. The bi-monthly samples represented about ten pounds of fresh glands.

During the past four years, 1914-1917, data have been accumulated on more than one hundred lots of desiccated thyroids from cattle, hogs and sheep which furnish the raw material for medicinal thyroid preparations. The samples were supplied by the factory and analyzed in this laboratory for control purposes.

Each of these lots represent many thousand glands and the collection time covered periods of several weeks. The animals furnishing the raw material came from all parts of the United States, with the exception of a few of the Eastern and Southeastern States. It is evident, therefore, that such factors as locality, feed, water, and particularly the considerable individual variation which is known to exist, have been satisfactorily eliminated. The fundamental causes for the fluctuations in the iodine content of the thyroid gland consequently must be temperature and weather conditions.

In the tabulation below are given the maximum and minimum iodine content of the thyroid glands collected during the two periods mentioned above and the yearly averages for the entire six years. All figures are calculated to a dry fat-free basis.

	Percent of Iodine in dessicated fat-free glands		
Time	1911-1913	1914-1917	Entire Period 1911-1917
Cattle:			
Maximum	0.43%	0.43%	
Minimum	0.04	0.04	
Yearly average	...	...	0.205%
Hogs:			
Maximum	0.47	0.38	
Minimum	0.17	0.15	
Yearly average	...	...	0.300
Sheep:			
Maximum	0.28	0.26	
Minimum	0.06	0.04	
Yearly average	...	...	0.150

It will be seen that the figures obtained during the last four years are almost identical with the earlier findings, as far as cattle and sheep are concerned. In case of the hog, the differences are more marked. This is in all probability due to the decreased number of hogs slaughtered during hot weather and the extended collection time.

The average iodine content of the hog thyroid,

taken year by year, is considerably above that of cattle and sheep. This may be of some significance, since the former is an omnivorous animal, while the latter are strictly herbivorous.

The seasonal variation in the size of the thyroid gland of cattle and sheep has been referred to above. Of these, the beef gland particularly is influenced by cold temperatures. It has been noticed year after year that the onset of severe cold weather is followed in a week or two by a noticeable enlargement of the cattle glands and consequent lowering of iodine content. This enlargment is less prominent or occurs later in mild winters than in severe ones. The glands of sheep are also quite sensitive to temperature changes, but not to the same degree as those of cattle.

Fluctuations in the yearly average iodine content of the thyroid gland also exists. These are naturally small and vary but a few hundredths of one per cent from year to year. They are undoubtedly due to weather conditions generally.

Where due allowances are made for climatic fluctuations and the differences in the time periods of collection, the last four years' results, when plotted out on paper, follow closely the curves published in previous reports.

SUMMARY

Additional evidence has been furnished to show that a distinct seasonal variation exists in the iodine content of the thyroid gland from cattle, hogs and sheep. The temperature factor is the most important of all in producing these fluctuations.

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CONFUSIONAL INSANITY AND THE OVARIES: A CASE HISTORY

George Howard Hoxie, A. M., M. D.,
Kansas City, Mo.

In the 1898 Edition of his *Psychiatrie*, Kraepelin states (1) that there is a close relation between menstruation and psychic disturbance, but that he inclined to the view that the relation was not causal.

In a symposium on the subject of the relationship between gynecologic and neurologic conditions before the Michigan State Society last spring, Reuben Peterson (2) held that there are four classes of patients to be considered, viz.:

"1. Women with neurologic symptoms whose pelvic organs are anatomically and physiologically normal.

2. Women with neurologic symptoms whose genital organs are anatomically normal but whose functions are abnormal.

3. Women with derangements of the nervous system whose pelvic organs are unquestionably diseased and where the disease may aggravate but does not necessarily cause the nervous manifestations.

4. Women of naturally good nervous organizations whose nervous manifestations have followed upon and hence apparently are due to true pelvic lesions."

This analysis is very useable, for it puts the crux where it belongs,—namely, in the antecedent condition of the nervous system. And in our study we should make this point our first determination.

Bandler (3) outlines a very comprehensive theory

as to the interaction of the ductless glands in gynecology. He lays great stress on the influence of the ovary on the pituitary, and seems to believe that definite psychical manifestations may result from ovarian insufficiency.

Auer (4) in 1915 expressed the opinion: "that the occurrence of insanity at puberty and adolescence after severe physical and mental strain and at the time of menopause,—all periods when the metabolic changes of the body are intense,—and the occurrence in syndromes unquestionably the result of disease of the glands of internal secretion of idiocy, imbecility, depression, mania and dementia suggest strongly that the true etiology of the effective psychoses lies in a junctional disturbance of the glands of internal secretion."

The best statistical study is perhaps that of Carey McCord (5), which he summarizes thus: "At the Michigan Home and Training School a survey has been made of 1,134 feeble-minded inmates for evidences of involvement of the internal secretory system in the defects of growth and development in the feeble-minded. Of the number examined, 240, or 21.16 per cent, presented the characteristics of various glandular syndromes. From our investigation the following inferences appear justified:

"1. Of the glandular cases seen in the feeble-minded, heredity stands out as the foremost factor in the etiology.

"2. The demonstration of syndromes in the feeble-minded does not in itself allow any inference that the feeble-mindedness is attributable to the glandular dysfunction. The glandular disease may determine the increasing defect, but more often the co-existing feeble-mindedness and glandular defect are both the outcome of a common cause.

"3. Promiscuous treatment of the feeble-minded with glandular derivatives is unprofitable and unwarranted. In established glandular types among the feeble-minded, more often glandular treatment is of no distinct and lasting value.

"4. In borderline cases of glandular disease with trivial mental inadequacy, glandular therapy may prove of special value. More often in these cases no true mental deficiency exists, and all manifestations of mental inadequacy are referable to the glandular mal-function. In such cases glandular treatment persistently carried out may be the factor deciding between normality and increasing defects."

In the following case we have some data not usually encountered, and they are given in the hope of making more definite our concept of the relation between ovarian secretion and neurologic condition. The psychic perturbations are well brought out in the transcription of the patient's own words.

Female, age 25, single, high school teacher.

Family History, without definite stigmata.

Personal History. Normal childhood. Menses at 12; since 14, painful. The pain is in the left side and begins before flow and lasts into second day. At 19 curetted and lay in hospital for three weeks. She had taken normal, college and university work, graduating with high honors. She had done special work in biologic research and won high commendation from the head of the department. She had taught in a high school two years with egneral satisfaction. Her statement of her scholastic life follows: "I was graduated from advanced course at the normal when I was seventeen. I did teach school in our little country school and stayed at home while teaching. When I entered

the university I was given junior credit plus ten hours. I completed both degrees B. A. and M. A. in two and a half years, graduating in nineteen-ten. The year following my entrance to the university I taught school at ———. While here I stayed with my sister, who was married when I was a mere child. When I was graduated from the normal Miss ——— told me to write, but not to attempt anything for publication until I was 35, but to write, write. She gave me a beautiful picture for having made the best average in the class. Prof. ——— told me to study sculpturing, Mrs. ——— wanted me to specialize in music. When I entered the university the zoology people wanted me to specialize in their department. Dr. ——— suggested that I try for the Bryn Mawr scholarship and said he would help me. The spring term of 1910 I assisted in zoology and was invited to join the zoology faculty meetings. That same spring I modeled chromosomes in clay with which to make candy chromosomes for the Sigma X banquet."

Her present complaint is of pains in the back of her neck and through the heart, and a backache, duration four or five weeks, but the patient is too confused to state her condition clearly. An aunt's letter follows:

"Nov. 29, 1913. ——— was engaged to be married and the date was set several times, but each time there was some excuse; once it was that she must help her brothers, by teaching school, to a profession of some kind. Then her poor health had been a reason. The young man has been very patient and I do not suppose realized that her mind had anything to do with putting the date off so many times. But he came to the conclusion it must be she did not love him

sufficiently and wrote to that effect and we think the engagement is broken. In those spells she says she is 'broken-hearted,' and nothing can take the 'pain out of her heart,' that 'no one cares or understands,' that 'no one belongs to her,' till it is very distressing, but she never mentions his name or tells us her trouble, but wants to make us think her worry is all about the boys' failure in life. My sister can see now that ———'s mind has not been entirely right for several years at times. And I suppose she has been suffering from this trouble since about fifteen or sixteen years of age. She has always been a great student, graduated from the ——— Normal and the State University; has taught school for several years and her pupils love her so much they always want her to come back. She tried it one week this fall but had to resign."

Status: 12. VII. 1913. Weight 132 (last year 130½). Nocturia and dysuria present. Neck shows enlarged thyroid (circumference 31.5 and 34 cm). Slight rotary nystagmus. BP, 85-109. Pulse, 108. Heart and chest negative. Right hypochrondrium slightly tender. Left groin very tender. Pushing on left leg causes pain in back. Uterus retroflexed, not tender. Bladder very tender. Tongue serrated. Urine: acid, 1028, indicanuria, many bacteria in fresh specimen, much epithelium. Blood: Hb. 80; Rbc. 5,600,000; Wbc., 15,300; polys. 64; monos. 25; eosin. 7, (amphophiles 22).

24. VII. 13. Entered hospital for treatment. T. 97.6, 98.4; P. 80-96; R. 20-24. BP. 80-100-110. Dysuria. Sleep poor. Has been weeping much at home. Twitches arrhythmically.

25. VII. 13. Under ether, uterus dilated, Naboth-

ian cysts opened, erosions curetted, etc. Left hospital after 10 days.

5. IX. 13. Office consultation. Still nervous. Nocturia. Pain in left hypochondrium. Neck 31 and 33 cm. Weight 131.

21. IX. 13. Patient's statement of condition:

"Pulse varies from 120 to 130. Pain in side—two distinct and separate pains, one a dull ache, the other sharper and feels as if part of my anatomy were contracting—brings me up with a start at times. Pain under ribs part of time. Pain in back nearly all the time. Pain in stomach has been very severe for some seven days. The sharp pains extend further down into the abdomen than formerly. My throat bothers me a very great deal—feels as if something were choking me. Red pimples occur all over my body. The slightest blow makes an ugly black spot. My skin is rough and dry and scales off constantly. * * * I have no ambition or enthusiasm—don't seem to care about living. It is horrible to feel this way. I am sure I don't understand why I do."

6. X. 13. From patient's statement:

"Condition of tongue—not as badly coated but more highly decorated around the edge. Appetite—none at all, but eat from sense of duty. Digestion is fairly good. Sleep—very restless and am forced usually to resort to sleeping tablets. Bowels act three or four times during day. Kidneys either act very frequently or rarely. In either case, the amount is small. There is always an action during the night and frequently three or four. Pain—not as much in stomach and under ribs. Pain in back and side is much the same. Opposite the heavy pain over my heart, there is a dull pain under the left shoulder

blade. I have been having a heavy dull ache in my head and when I stand it becomes a throbbing pain accompanied by dizziness. When I was ill last week I suffered very much with pains in my side and back. There was no flow but a discharge."

4. XI. 13. Daily weeping—sobbing—nightmares. Weight 127. Pain in left sacral region most of the time. Coarse tremor of hands and tongue. Pain in left groin when defecating. Neck 30.5 and 32.5. Urine full of bacilli (motile) with pus.

12. XI. 13. From patient's statement:

"I was so tired and weak when I arrived in ——— that I sank almost at once into a comatose state. The last thing I remembered was vigorously and emphatically protesting with the girls not to send for you—I knew I would be all right in the morning. I felt this manifestation of coma enveloping me when I was in your office—I think it was this condition of mind that made me so stupid. Uncle (fictitious—G. H. H.) says you understand why I always exhibit my very worst self when I get nervous and that I must not worry about it, that it will come out all right, when I get less nervous and stronger. He's such a comforting Uncle. I have been having a little fever each day since coming home. Since beginning the medicine and enemas I have suffered with severe burning pains very low down in the abdomen. The pains are more severe when the kidneys act. They act six or seven times during the night."

30. XI. 13. Mental condition worse rather than better—confused. Visions of father who had died two years before. Indicanuria persists with bacilluria. Re-enters hospital.

2. XII. 13. Endometritis with profuse secretion.

Rectum still inflamed. Renal excretion of phthalein 28% in 1 hr., 56% in 2 hrs.

Blood: Hb. 90, Wbc. 7500, polys. 80, eosin. 5, monos. 22 (amphophiles 22%). Urine culture, staphylococcus.

8. XII. 13. Hysterical delirium caused by mother's visit.

17. XII. 13. Tenderness in left hip persists; it seems to include both muscles and bones.

29. XII. 13. Cervix practically normal.

1. I. 14. Tenderness in left groin very slight. Patient cannot bring her fore fingers together with eyes shut.

10. I. 14. Still indicanuria. Earthy phosphates.

22. I. 14. Better but cannot collect thoughts or remember recent events. Still visits her father in her dreams. Still has far-away look in her eyes. Pain in side and headache after exercise.

14. III. 14. Just returned from spending a month in a sanatorium for mental disease. The contact with the really insane has brought about self-control. She still feels a "hurt inside" which she cannot explain and thinks that it has been there since father's death. No memory of her last few years.

A letter about April 28, 1914, gives her own statement of her symptoms thus:

"At night I am afraid to go to sleep and afraid to remain awake. My heart and soul are so hurt that I don't feel I can endure it much longer. When I do sleep I dream Miss ———, mother and you stand around my bed exclaiming in derision, 'You are not a truthful person; we don't trust you; you are not good like your friends,' and oh! the scorn in your voices. Then, often I plead with you to believe in me and

show me what to do, you all refuse and desert me. At this point I find myself screaming or sobbing.

"I was beginning to feel so much better the last few days I was in Colorado. But nothing seems to help the weight in my head now. I am out doors nearly all day working in my garden. I work until I can endure the feeling of wrong doing no longer, then I have to cry it out and begin over again. I never have a moment's peace. I am beginning to think I shall never be a normal person again. I have forgotten how to smile or be able to bring joy to anyone. I am so wretchedly unhappy—I find myself imagining all kinds of things about myself that would make me different from good people.

"The last time I menstruated I began to menstruate four or five days too soon. The nature of the discharge indicated I had taken cold some way. I am so dizzy-headed, have a bad taste in my mouth and have very sluggish bowel action and bad stomach."

10. IX. 14. Her mythical uncle still "writes" to her.

4. XII. 14. Menses accompanied by a delirium. Relieved by corpus luteum. Urine negative. Is a pupil nurse in a hospital.

9. IV. 15. Has lost 25 pounds. Now has sore throat and grip.

4. VIII. 15. Pain in left kidney, with frequency and painful micturition.

2. IX. 15. Laparotomy—Hertzler—A fibroma of the round ligament 3.5 cm. in diameter removed. Left ovary senile. Right only slightly better—neither removed.

5. IX. 15. Culture of urine shows a Gram negative bacillus still present.

25. IX. 15. Constant back and left side ache. Wobbly on her feet. Troubled by dreams.

10. XII. 15. Left kidney and ureter still tender.

23. II. 16. Patient requires corpus luteum at every menstrual season. Mental confusion present but can be controlled by this remedy.

30. I. 17. Weight 144½. Still shows nervous weakness at menstrual season, but can do her work Backache and left side ache.

18. IV. 17. Frequent micturition. Sore throat Tired out. Mentally clear.

13. IX. 17. Blood: Hb. 100; Rbc. 4,600,000; Wbc. 9000; polys. 71; eosin. 3; monos 25. Vaccinia with infected arm. Mentally clear.

SUMMARY

A young, university-bred woman who has always suffered from dysmenorrhea, practically since the onset of puberty, after teaching in a high school for two years, alarms her friends on account of her mental imbalance. Her own account of her condition would place it among the melancholias. But her physical condition is also bad on account of neglected pyelitis and cervicitis and constipation. Treatment for her physical condition, with rest in a convalescent home, slowly brought her out of her melancholia. But not until corpus luteum was given at the menstrual season did she clear up sufficiently to make herself practically useful. The monthly attacks are of the confusional nature—melancholy because confused. The young woman is now successfully carrying on her chosen work.

DISCUSSION

In this case the connection between the ovarian dysfunction and the mental confusion was incontro-

vertible. The other physical conditions—the backache, the pyelitis, the vaccinia, etc.,—came and went without disturbing the patient's mental condition. But the ovarian dysfunction produced regularly the mental confusion. The mental confusion seemed to disappear as regularly upon the administration of corpus luteum (either H. W. & D.'s "lutein," or P. D. & Co.'s ampoules of soluble extract). The patient grew steadily stronger and the attacks of confusion more fleeting, so that at the end of the story she was not incapacitated for work at any time during the menstrual cycle. We were rather slow in arriving at this conclusion, and worked first on the hypothesis of its being a base hyperthyroidism. Then, as this syndrome disappeared, we thought of Freud's theories; and then, as the mind became clearer, of simple hysteria. But in the end when all the complicating symptoms subsided it seemed clear that the disease was of the confusional type and due to atrophic ovaries.

The interesting finding of the very rare fibroma of the round ligament, and its removal, seemed to have very little bearing or influence on the mental condition, although the operation relieved some of the dysmenorrhea.

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DIABETES INSIPIDUS

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Diabetes insipidus has for centuries been recognized as a distinct clinical entity, the main symptom of which is polyuria without pathological content in the urine. The etiology, however, has been obscure.

Older writers have distinguished between an "idiopathic" and a "symptomatic" form, while more recent authors have sought by the functional kidney tests to establish a distinct division between primary polyuria and primary polydipsia. It has also been suggested to reserve the term diabetes insipidus for the "true" cases, that is for the primary polyurias due to an insufficient ability of the kidneys to produce a concentrated urine.

During recent years new viewpoints have been advanced of far reaching significance for the conception of the etiology and pathology of this disease, — views that have been reflected in the therapy, which at present seems to be more promising than has previously been the case. Although many obscure questions remain to be solved, it now appears justifiable to classify the disease as a disorder of the pituitary body. There are many cases in which this cause is beyond doubt, and probably the majority of the "true" diabetes insipidus cases will turn out to be of pituitary origin.

It has long been known that polyuria often occurs after traumatic lesions of the skull, and that it is a frequent symptom of certain nervous diseases, organic as well as functional.

Claude Bernard's celebrated piqure (1854) threw some light upon these facts, and he believed that he had discovered a "centre" for diabetes insipidus. Later investigations, however, have shown that polyuria will result from lesions of many other parts of the nervous system.

These observations gained in importance, as Magnus and Schäfer (1901) showed that the pituitary extracts had certain diuretic properties. This statement has led to considerable confusion and it has but recently been recognized that the effect really is antidiuretic.

Clinically the direct relationship between diabetes insipidus and the pituitary body was first pointed out by Frank (1912), and during the few years that have elapsed since, similar cases have been reported where this relationship is unquestionable.

As far as our present, limited knowledge goes, the most frequent pathological findings are tumors, syphilis and tuberculosis.

The pituitary adenomas, which are the most frequent causes of acromegaly, only exceptionally lead to polyuria, and little is known about the effect of the pituitary cysts. In most of the cases there have been found malignant tumors, either of the neighborhood, secondarily involving the pituitary, or in the gland itself. Metastases from cancer are especially prone to locate in the hypophysis.

The frequency of a syphilitic history in these cases has long been known. Anatomically the usual finding is syphilitic basal meningitis. This probably in some way interferes with the functional activity of the hypophysis. In a few instances there were syphilitic lesions of the gland proper.

In many of the cases of diabetes insipidus on record the patients have been suffering from pulmonary tuberculosis, but this fact has not attracted much attention. Of recent years careful anatomical investigations, however, have shown actual tuberculosis of the pituitary body, sometimes with total destruction of the gland.

These changes are easily overlooked, and in some cases the lesion has not been discovered until the microscope has revealed it. Negative findings, where the hypophysis has not been specially examined, therefore, amount to little.

There are, furthermore, as I have reason to believe, a certain number of cases due to atrophy or congenital hypoplasia of the gland. It is well known that polyuria often sets in during or after acute infectious diseases, and also how apt the ductless glands in general are to be damaged by infections. It is a common experience, gained in experimental as well as in clinical surgery of the hypophysis, that polyuria often occurs after removal or injury to the gland.

Most writers on this subject have supported the theory that these conditions have acted as stimuli for the pituitary, in accordance with the views of Magnus and Schäfer. But as there are some cases where the entire gland has been destroyed, we are obliged to drop this hypothesis and assume a hypo-function of the gland. Some cases have shown a total destruction of the posterior lobe, while the anterior has remained intact.

During the past four years, or since attention has been directed to the pituitary body as concerned in this disease, there has not been reported a single

autopsy finding in which this gland has not been in some way involved.

These cases are not numerous and they are scattered in the literature of many countries, and a presentation of the features common to them has not yet been given. By making retrospective diagnosis in the older diabetes insipidus literature I have been able to add a number of cases where the pituitary origin can be regarded as pretty well established. On this basis I will now outline some features of the clinical picture. It has been surprising to see how relatively clear-cut and uniform this condition is, when facts which were previously considered of minor importance are taken into account. The picture is in general agreement with what the textbooks give as the symptoms of diabetes insipidus, without any regard to the pituitary origin. Adiposity is frequently mentioned, but it seldom reaches any extreme degree. In the few cases where it has been tested, there has been found a high carbohydrate tolerance. Almost as common as adiposity is sexual underdevelopment, the degree of which will be dependent as well upon the seriousness of the disease as upon the age at the onset. If the polyuria sets in during childhood, puberty will very likely be delayed or entirely lacking and the patient remain in a more or less pronounced infantile state. When the onset has come in adult age, regressive changes in the sexual organs have sometimes been noted. Impotency and amenorrhoea are among the most constant symptoms, and usually set in simultaneously with the polyuria which in most instances starts quite suddenly. The secondary sex characteristics show the same changes. The growth of hair in the

armpits and on the pubes is scanty, and even marked loss of hair may come on shortly after the onset, though this is comparatively rare. The growth of the beard is apt to be scanty and slow, while there are usually no changes in the hair on the head, and the eyebrows are also intact. This last mentioned fact is in distinction from hypothyroidism, where the "eyebrow sign" is said to be of value.

These patients usually suffer from constant fatigue and are troubled with a never-ceasing lassitude; in other words there is a more or less marked asthenia. In many cases psychic alterations also take place, such as somnolence and apathy, sometimes accompanied by depression and melancholia.

The skin is usually dry and these patients perspire very little. Another valuable sign is the slightly subnormal temperature. Apart from these general manifestations there are certain symptoms which are directly pointing to the hypophysis, such as enlargement of the sella turcica and bitemporal hemianopsia. Neither of these findings are very frequent, and negative results do not speak against the pituitary diagnosis. The combination of polyuria and hemianopsia has long been known, and the visual disturbance is often of a peculiarly short duration, the *hemianopsia fugax*. All the distressing symptoms of an intracranial tumor may of course be seen in some cases.

It could not be expected to find all or even the majority of the above mentioned symptoms and manifestations in each case. However, I believe it will be very rare, in cases of primary polyuria, not to find anything pointing towards the pituitary body. There seem to be two fairly distinct types: the obese,

indolent; and the lean, infantile type. The family history does not give definite information, although some instances have shown a pronounced hereditary tendency. The complaint, which causes the patient to consult the doctor, is almost invariably polyuria, but when the degree is only slight the most distressing feature has been weakness or headache, and very rarely, eye troubles.

This varying picture will naturally suggest a disease of different ductless glands, but space will not permit me here to enter into a discussion of the intimate relationship between these glands. However, all of these signs can, with apparent probability, be referred to the hypophysis.

As mentioned, pathological experience has shown that it is no longer permissible to assume an excess of pituitary secretion. It will therefore be of interest to see how the disease compares with the hypofunction of the gland. The picture of this condition has of late been brought out in an admirably clear way,—by Cushing's work especially. It is sufficient to point out what he regards as the four cardinal symptoms:

1. High carbohydrate tolerance.
2. Subnormal temperature, slow pulse, low blood pressure.
3. Drowsiness and sleepiness.
4. Asthenia.

Anhidrosis, scanty growth of hair, sexual hypoplasia, impotency and amenorrhoea also belong to the picture, and it is now pretty well established that Froehlich's syndrome, the dystropia adiposo-genitalis, is due to hypopituitarism.

The correspondence is so striking and obvious indeed, that further comment is unnecessary. Here I

wish, however, to emphasize that it is not unusual to see very marked cases of adiposo-genital dystrophy or other cases of hypopituitarism with a normal output of urine. The functional activity of the posterior lobe seems to be well specialized.

Usually the diagnosis is easy when the conditions just emphasized are taken into consideration.

It is doubtful whether a subcutaneous injection with some pituitary extract is of diagnostic value, as the antidiuretic effect seems to be a general physiological action, not limited to the cases of pituitary insufficiency.

Psychic treatment or forced restriction of water, sometimes valuable in primary polydipsia, has not proven efficacious in "true" cases. A diet poor in chlorides and nitrogen has been the main treatment and has been able to lower the output to a certain extent. On the whole, however, the treatment has been rather unsatisfactory; none of the drugs recommended is of special value. Opium will sometimes decrease the thirst and in that way lower the output without exerting any influence on the concentration. The only remedy which has power to check polyuria and concentrate the urine is the extract of the posterior lobe of the hypophysis. A subcutaneous injection with an ampoule of some of the usual commercial preparations will probably be sufficient to exert a very marked influence on the output. This effect will usually show in a few hours and reach its maximum in 4-5 hours. Unfortunately the effect is not lasting and the output will probably be high again the next day. There are, however, cases on record where the diuresis has been checked for weeks afterwards. The injections are well borne; paleness,

slight headache and ringing in the ears may occur, but only last for a few hours.

Intravenous injections are not advisable as they may lead to collapse.

As this treatment cannot be kept up for a long period, it would be a great advantage if treatment by mouth might prove of some value. This mode of administration is far less efficacious, but is without discomfort and, as far as our present knowledge goes, is free from danger, even in large doses. Such treatment, therefore, can be carried on indefinitely.

The sufficient dose has to be tried out in each case, and as a rule very large doses are required, the amount of active material absorbed from the intestinal tract being evidently very small. The commercial dry preparations will very likely prove inefficient. Wherever possible the treatment should be tried with fresh material from the abattoir, as well for economical reasons as for the fact that the dried preparations are less potent. As it is very difficult, at least in pronounced cases, to check the 24 hour amount of urine in this way, it will probably be the best plan to confine the therapeutic aims to securing a normal output during the night and thus relieve the patient of one of the most distressing features—the restless nights.

One patient who has been under my care for the past two years has been very much improved by an intermittent pituitary feeding. She has taken from two to seven fresh pituitary bodies from cattle every evening. The output has hereby been checked during the night,—usually decreasing from nearly 2500 cc. to approximately 300 cc. At the same time the general state of health has improved consider-

ably, adiposity and drowsiness having disappeared, and menses have been re-established. Feeding the anterior lobe alone does not lead to this effect. This patient also shows another interesting feature. At present one hypophysis will have the same effect as, two years ago, could not be obtained by less than seven glands. The most satisfactory explanation of this fact will probably be that the hypophysis of the patient during the functional rest by the extraneous help has gained in secretory ability. This would be analogous to the explanation of the increased sugar tolerance in diabetes mellitus after alimentary rest, and is more in harmony with the laws of general physiology, than the usual assumption that the pituitary extracts stimulate the pituitary body.

This is an entirely new field for organotherapy, and only the future can tell how many cases will be benefited by treatment along these lines.

In the syphilitic cases an energetic antiluetic treatment will often prove of lasting value. The cases due to tumor have to be treated according to general surgical principles. In one case where the patient presented some evidence of brain tumor, the output was checked by a lumbar puncture.

As previously mentioned there has been confusion as to the effect of the pituitary extracts on the flow of urine. Recent clinical investigations, and among them my own work, have, however, shown quite definitely that the extracts from the posterior lobe physiologically serve to secure a normal concentration of the urine. I have gone more deeply into this question experimentally and my results indicate that this action is exerted on the sympathetic nervous system, especially on the vaso-motor nerves for

the renal vessels. These results may lead to a broader view of the polyurias. When the sympathetic system does not get its normal stimuli, as is the case in organic lesions with destruction of the posterior lobe of the pituitary body, polyuria will result. In functional disorders of the nervous system polyuria of varying degree and duration is frequently seen. The most satisfactory explanation in these cases seems to be to assume a temporary lack of tone of the vasomotor fibres in the sympathetic nervous system. The "urina spastica" of the old observers is probably rather a "urina atonica," indicating a lowered tone of the renal vaso-constrictors. Possibly these pathological polyurias of varying severity and of apparently different origin, ranging from the occasional polyuria of the neurotics to the polyurias of extreme degree in diabetes insipidus, can be linked together by the sympathetic nervous system.

Though this field is in urgent need of further investigation, it has become clear that diabetes insipidus is merely a symptomatic evidence of disordered pituitary function, and that it is due to a deficit of secretion. In consequence, administration of pituitary preparations will be the proper therapy.

VASCULAR CHANGES PRODUCED BY ADRENALIN IN VERTEBRATES

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The majority of physiologists still teach that adrenalin is essentially constrictor in its effect upon the blood vessels, ignoring the fact that doses which are probably physiological in their magnitude cause dilatation in a large proportion of vessels. These teachings are founded upon the older experiments in which massive doses of the hormone were used. Such amounts of adrenalin are probably never secreted by the adrenal glands (1, 2, 3). Although in the last few years it has been conclusively proven that small quantities of adrenalin cause vasodilatation and a fall in blood pressure as a result (4, 5, 6, 10) the fact is still ignored. This situation may be easily explained, for, among the common laboratory mammals some give evidence of vasodilatation while others consistently fail to do so. These animals which have been found to give positive proof of dilatation belong to the carnivores, while those that do not belong to the rodents. In face of the experimental facts it was as easy to believe the response of cats and dogs exceptional, as that the effect in rabbits was different from that in other animals. In view of this disagreement, it was perfectly natural to assume that the action of adrenalin in cats and dogs was unusual, since it did not conform to other beliefs such as the absence of vasodilator fibers in the sympathetic nervous system.

This research was undertaken with the object of determining whether the dilator action of adrenalin was confined to the carnivores. It was conceivable that other groups might give a similar action, although none were known to do so; accordingly a survey was made of all the groups available. The results have been sufficient to remove all doubt as to the general occurrence of vasodilatation from adrenalin.

A brief sketch of our present knowledge concerning this dilatation is needed as a foundation for this research. The nature of the mechanism on which adrenalin acts was worked out largely by experiments upon cats and dogs. Those experiments have proven that a differential effect is produced—dilatation in skeletal muscle (5, 6) and intestine, (large doses)—constriction in skin (6), intestine (small doses), kidney (8, 10), bone (16), thyroid (15) and spleen (7, 10). With small doses, the vessels in skeletal muscle more than counteract the constriction in the skin and abdominal viscera, so that a fall in blood pressure results. When the amount of adrenalin is sufficiently large, the constriction of skin and visceral vessels (excepting intestine) becomes great enough to more than compensate for the dilatation in skeletal muscle, thus producing a rise in blood pressure.

The dilatation produced by adrenalin has been shown to be brought about by dilator mechanisms located in the sympathetic and dorsal root ganglia (12) as well as in a "terminal" receptive substance which has been called the myoneural junction (13, 14). The latter, a counterpart of the constrictor myoneural junction, is assumed to be associated with dilator fibers.

METHODS

The methods employed in this research were those already described in work from this laboratory (10, 11, 12).

All animals, unless otherwise stated, were anaesthetized with ether. Blood pressure was taken from the carotid artery, except in the fowl, in which case the sciatic artery was used. Injections were made into the jugular vein.

Solutions of adrenalin chloride were made up by diluting the 1:1,000 preparation of Parke, Davis & Co. Volume changes were registered by means of Brodie's bellows. The plethysmograph for the limb was either of the type which enclosed the paw, or else like a cuff, so that the paw might be excluded (13). It was necessary to use artificial respiration in the fowl when the abdomen was opened.

RESULTS

Reptilia (Chelydra)

A snapping turtie (5.3 kgm.) was employed as representative of the reptiles. Doses of adrenalin as small as 0.2 c.c., 1:1,000,000 were tried with no effect upon the blood pressure. Even 0.5 c.c., 1:100,000 had no effect. 1.0 c.c., of the latter concentration caused a rise from 46 mm. to 50 mm. 0.4 c.c. 1:10,000 caused a change from 44 to 54 mm. 1.0 c.c. of the same solution produced about the same effect. Indeed it was found that with large doses, sensitiveness to adrenalin was soon lost. 0.5 c.c., 1:1,000 following the above, increased the pressure only 6 mm. from 51 mm. Repetition of this had no effect, nor did twice the dose. Two months later, the blood pressure and intestinal effects were studied in the same animal. The blood pressure responses were similar. The in-

testine always gave constriction when there was any effect. This was observed with doses ranging from 0.5 c.c., 1:100,000 to 3.0 c.c., 1:10,000. After the latter dose, 1.0 c.c., 1:1,000 produced no intestinal change.

Although only tentative conclusions can be drawn from a single animal, they are at least valuable when considered in connection with other vertebrates low in the scale. We have found that the vascular system of the turtle is not very sensitive to adrenalin and that there is evidence of only a constrictor mechanism. The failure to obtain a fall in blood pressure or a dilatation of the intestine indicate an absence of the dilator mechanisms.

Aves (Gallus)

The fowl serves as an example of the warm blooded vertebrate other than the mammal. It is much more sensitive to adrenalin than are the cold-blooded vertebrates. Moreover it does not easily lose its power to respond to this hormone, even after numerous doses.

Constriction is the only effect produced by adrenalin in the fowl. Both the limb (Fig. 1) and the intes-

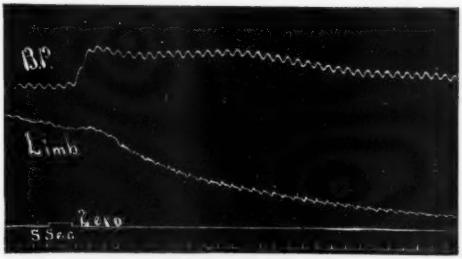

FIG. 1
Effect of 0.5 c.c., 1:100,000 adrenalin upon the limb in the fowl, 1.0 kgm. (Reduced ⅔.)

tine (Fig. 2) respond in this way. From a study of

FIG. 2
Prolonged constriction of the intestine in the fowl. (0.92 kgm.)
Produced by 0.5 c.c., 1:10,000 adrenalin. (Reduced ⅔).

seven animals no evidence of the existence of the adrenalin vasodilator mechanisms (Table 1) has been found.

TABLE I.
RESPONSE TO ADRENALIN IN THE FOWL

Weight in kgm.	Dose	Blood pressure change in mm. of mercury	Limb	Intestine
1.1	0.2 cc 1:1,000,000		Slight constriction	
	0.5 cc 1:100,000	109-138	Constriction	
	1.0 cc "	114-182	Marked constriction	
1.0	0.1 cc 1:100,000	118-130	Constriction	
	0.5 cc "	106-134	Marked constriction	
0 92	0.2 cc "	65- 79	Constriction	Constriction
	0.5 cc "	95-175		Marked constriction
0.85	0.2 cc 1:1,000,000	52- 54	Constriction	
	0.5 cc 1:100.000	55- 65	Marked constriction	Constriction
	1.0 cc "	80-119		Constriction
0.95	0.5 cc 1:100,000			Constriction
	0.5 cc 1:10,000			Very marked constriction

MAMMALIA

Marsupialia (Didelphys)

A single opossum about two-thirds grown (weight 1.3 kgm.) was used in this research. A fall in blood

pressure (Fig. 3) was easily obtained from adrenalin.

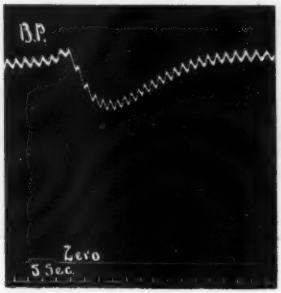

FIG. 3
Blood pressure fall in the opossum produced by 0.2 c.c., 1:100,000 adrenalin. (Reduced ⅝.)

This was usually preceded by a brief rise. With larger doses pure pressor effects resulted.

Although the limb included in the plethysmograph possessed a smaller proportion of muscle than that in most mammals it gave active dilatation (Fig. 4) ex-

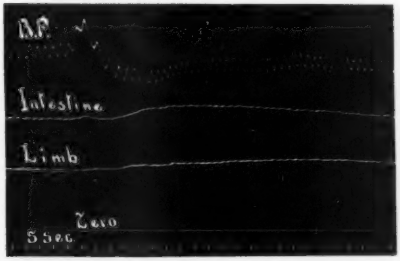

FIG. 4
Dilatation of limb and intestine in the opossum caused by a depressor dose of adrenalin, 0.2 c.c., 1:10,000. (Reduced ⅝.)

cept when large doses were used. The intestine dilated actively in response to adrenalin (Fig. 5), the dilatation becoming very marked with large doses (Table II).

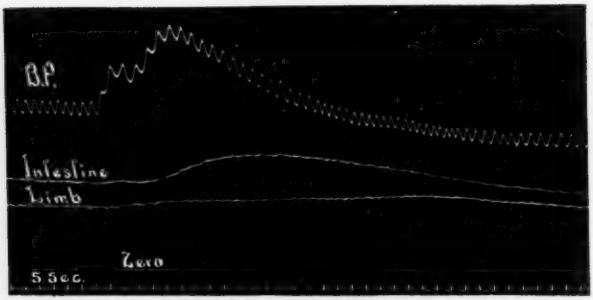

FIG. 5
Marked dilatation of the intestine in the opossum resulting from the injection of a presser dose of adrenalin 0.5 c.c., 1:10,000. (Reduced ⅝.)

TABLE II.
RESPONSE OF THE OPOSSUM TO ADRENALIN

Dose	Blood pressure change in mm. of mercury	Response of limb	Response of Intestine
0.05 cc 1:100,000	140-142-136		Dilatation
0.1 cc "	138-144-128		Dilatation
0.2 cc "	144-151-135	Slight constriction	Dilatation
0.5 cc "	118-125-106	Dilatation	Constriction and dilatation
0.5 cc 1:10,000	123-180	Small dilatation	Marked dilatation
1.0 cc "	98-215	Small dilatation	Marked dilatation

We may conclude then that the opossum and probably all marsupials possess adrenalin vasodilator mechanisms similar to those in the cat and dog.

UNGULATA

Perissodactyla (Equus)

Unfortunately the horse which we used was in such poor condition that it cannot be considered typical. It was anaesthetized with chloroform, and 1:1000 adrenalin was injected in every instance. In no case was there a fall in blood pressure. 5.0 c.c., adrenalin changed the pressure from 114 mm. to 162 mm.

10.0 c.c. increased the pressure from 80 to 260 mm.

Attempts to produce dilatation of the intestine were successful when 25.0 c.c. was injected, there being a strong constriction followed by a dilatation. 20.0 c.c. produced constriction only.

Intestinal dilatation was the only indication of the presence of an adrenalin vasodilator mechanism in the horse.

Artiodactyla (Capra)

In view of the unsatisfactory condition of the horse, it was imperative that another animal belonging to the ungulates be tried. An experiment with a goat (weight 13.0 kgm.) removed all doubt as to the existence of adrenalin vasodilator mechanisms in this order. A depressor effect (Fig. 6) as well as

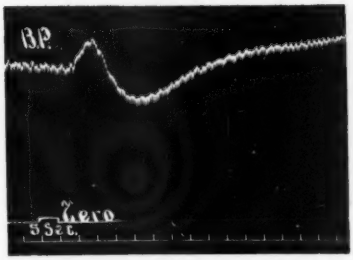

FIG. 6
Fall in blood pressure from 0.4 c.c., 1:100,000 adrenalin in the goat, 13.0 kgm. (Reduced ½.)

active dilatation of the limb (Fig. 7) could be obtained from the injection of small amounts of adrenalin. However nothing but constriction in the intestine (Fig. 8) resulted from even large doses of adrenalin until perfusion was attempted. A loop of intestine, with nerves intact, but shut off from the general circulation and perfused with oxygenated Ringer's solution gave pronounced dilatation both when

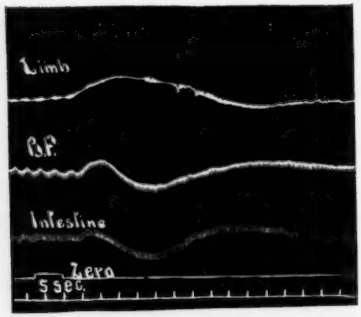

FIG. 7
Dilatation of the limb and constriction of the intestine produced by 0.5 c.c., 1:100,000 adrenalin in the goat. (Reduced ⅓.)

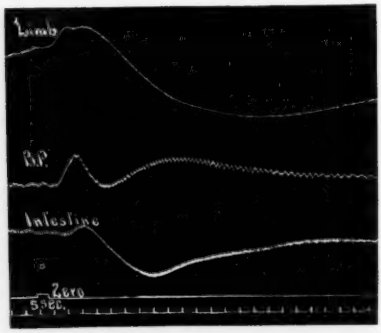

FIG. 8
Constriction in the limb and intestine caused by 1.0 c.c., 1:10,000 adrenalin, goat. (Reduced ⅜.)

TABLE III.
RESPONSE OF THE GOAT TO ADRENALIN

Dose	Blood pressure, mm. of mercury	Change in Limb	Change in Intestine
0.4 cc 1:100,000	110-128-94	Dilatation	
0.5 cc "	62- 68-53	Dilatation	Constriction
0.7 cc "	72- 80-61	Dilatation and Constriction	Constriction
0.3 cc 1:20,000	80- 92-66	Constriction	Constriction
1.0 cc "	84-106	Constriction	Constriction
1.0 cc "	28- 26		Dilatation*
2.0 cc "			Dilatation*

*Intestine perfused.

1.0 c.c., and when 2.0 c.c., 1:20,000 adrenalin were injected into the jugular vein. (Table III).

Our experiments thus indicate that the mechanisms for dilatation from adrenalin are found in the ungulates.

CARNIVORA

Cats and dogs were the only Mammals known to possess adrenalin vasodilator mechanisms before this research was undertaken. We were interested in finding out whether all families in this order reacted to adrenalin in the same way. Two other families were therefore investigated, viz.—the *mustelidae* and the *procyonidae*.

Mustelidæ (Putorius)

Study of an old ferret (weight 0.6 kgm.) indicated the presence of the vasodilator mechanisms. This evidence was largely limited to depressor effects of adrenalin, 0.2 c.c., 1:1,000,000 causing a fall of 6 mm. from 152 mm. In one instance dilatation of the limb was obtained.

Procyonidæ (Procyon)

Typical adrenalin vasodilator effects were obtained in the raccoon. A marked fall in blood pressure was produced by small doses. (Fig. 9). Dilatation of

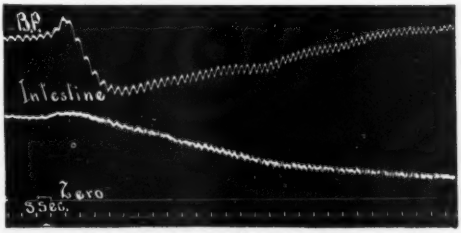

FIG. 9
Fall in blood pressure and constriction of the intestine produced by the injection of 0.2 c.c., 1:100,000 adrenalin. Raccoon. (Reduced ⅝.)

the limb sometimes resulted from depressor doses. Constriction (Fig. 9) or constriction and dilatation (Fig. 10) occurred in the intestine depending upon

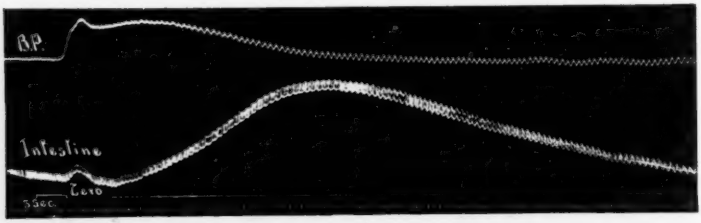

FIG. 10
Dilatation of the intestine produced by 0.3 c.c., 1:10,000 adrenalin, raccoon. (Reduced ⅔.)

the amount of adrenalin injected, just as in cats and dogs.

RODENTIA

A reason already given that the cat and the dog have been considered possibly exceptions in their behavior toward adrenalin is the fact that the rabbit does not give the same results. We will show, however, judging from the rat and rabbit that rodents are an exception in their behavior toward adrenalin and that the reaction of the cat and dog is the typical one for most mammals.

Muridæ (Mus)

A fall in blood pressure could not be obtained in the white rat. In an animal weighing 0.23 kgm., 0.05 c.c., 1:100,000 adrenalin caused a pure rise from 69 to 83 mm. Smaller doses such as 0.3 c.c., 1:1,000,000 had no effect.

Leporidæ (Lepus)

We have never obtained evidence of the presence of adrenalin vasodilator mechanisms in the rabbit. At least twelve rabbits have been examined in this

connection. It has always been our experience that whenever a dose of adrenalin is large enough to produce any effect, nothing put a pure rise of blood pressure results.

There might, however, be a differential effect without a fall in blood pressure. In one experiment the coeliac, superior mesenteric, inferior mesenteric and renal arteries were tied (5) without changing the reaction to adrenalin.

The limb reaction was determined in four animals. With small doses a dilatation which appeared to be passive, sometimes occurred. When the amount of adrenalin was increased constriction was produced. (Fig. 11). The presence of active dilatation was

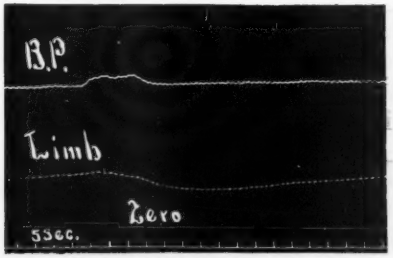

FIG. 11
Constriction of the hind limb of a rabbit (2.4 kgm.) from 0.4 c.c., 1:100,000 adrenalin. (Reduced ½.)

then sought in another way. The hind limb of an animal was perfused with Ringer's solution, and adrenalin was injected into the jugular vein. If dilator mechanisms sensitive to adrenalin, exist in the sympathetic and dorsal root ganglia, the limb under these conditions should respond. The injection of even large doses of adrenalin into the jugular vein was without effect. Injection into the perfusion fluid as it entered the iliac artery was also without

effect in one animal, while in a second rabbit the first two doses (0.5 c.c. and 0.1 c.c., 1:100,000) caused constriction, but later doses had no effect.

In one experiment the sciatic and femoral nerves in one limb had been cut seventeen days before. However no evidence of a terminal dilator mechanism could be obtained. In the cat and dog this has been obtained easily by such a method (13, 14).

Very small passive dilatations were produced in the denervated limb of the rabbit when adrenalin was injected into the general circulation. This limb was perfused later, doses of adrenalin varying from 1:1,000,000 to 1:10,000 concentration being injected into the fluid, but without result.

The reaction of the intestine was observed in four animals. In one, there was small passive dilatation with small doses. The other three constricted with doses of this size. In all there was prolonged constriction with large doses (Fig. 12). As an illustra-

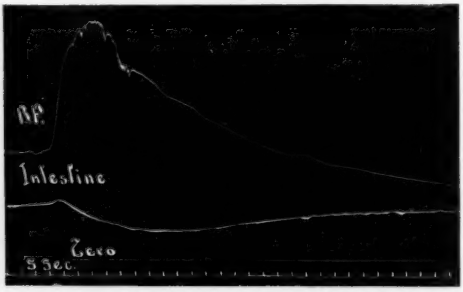

FIG. 12
Constriction of the intestine of a rabbit due to the injection 0.5 c.c., 1:10,000 adrenalin. (Reduced ⅔.)

tion of the amount of constriction; a loop 37 c.c. in volume constricted .72 c.c. after the injection of 0.5 c.c., 1:10,000 into the general circulation.

In an unpublished research we have found that there is a dilator mechanism for the kidney located in the aortico-renal ganglion. One of the methods employed has been to apply adrenalin solutions to the ganglion, noting the volume change in the kidney. We did this in a rabbit, but obtained constriction in the kidney instead of dilatation.

We conclude from our results that rodents do not possess adrenalin vasodilator mechanisms.

PRIMATES

Monkey (Pithecus)

Adrenalin vasodilator mechanisms are present in the monkey (Table IV). Excellent dilatations of a

TABLE IV.
RESPONSE OF THE MONKEY TO ADRENALIN

Dose	Blood pressure change in mm. of Mercury	Limb	Intestine
0.1 cc 1:100,000	96-101-92	Dilatation	Constriction and slight dilatation
0.4 " "	94- 98-86	Dilatation	
1.0 " "	80- 98	Very marked dilatation	
0.3 " 1:10,000	86-124	Marked dilatation	Marked constriction and dilatation
1.3 " "	64-166	Marked dilatation	Marked constriction and dilatation
2.5 " "	64-177	Marked dilatation and constriction	Marked constriction and dilatation

leg were produced (Figs. 14 and 15) by doses of adrenalin ranging from 0.4 c.c., 1:100,000 to 0.7 c.c., 1:10,000 (weight of animal 5.2 kgm.) (The foot was not included in the plethysmograph). Indeed, a large dose of adrenalin was required to cause reversal in the limb (Fig. 16). By perfusing the limb and injecting adrenalin into the jugular vein we attempted to bring the gangliar mechanism into action, without

result. We thought this might be due to failure of the adrenalin to reach the ganglia on account of

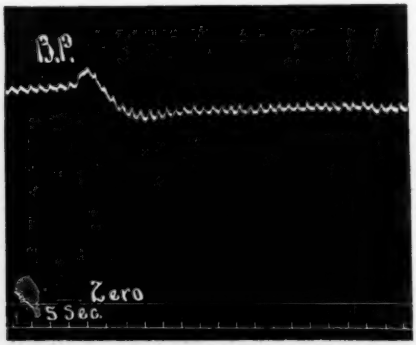

FIG. 13
Fall in blood pressure in the monkey (5.2 kgm.) resulting from 0.4 c.c., 1:100,000 adrenalin. (Reduced ½.)

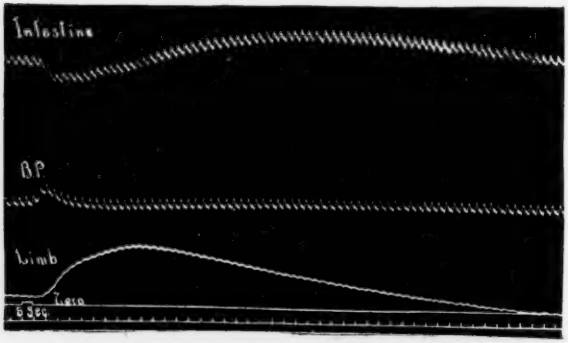

FIG. 14
Response to 0.5 c.c., 1:100,000 adrenalin in the monkey. Constriction followed by dilatation of the intestine. Marked dilatation of the limb. (Reduced ⅔.)

clamping the aorta too high up, as that has frequently been the case in cats. On the other hand injection of the hormone into the perfusion fluid easily produced dilatation. The explanation, therefore, might be that the vasodilator myoneural junction and not the gan-

gliar mechanism was the source of the dilatation. We are inclined to doubt this as being typical, for there is no reason to believe that the monkey is different from the cat and dog in which the gangliar mechanism is an important source of adrenalin vasodilatation (13).

The intestinal mechanism in the monkey worked

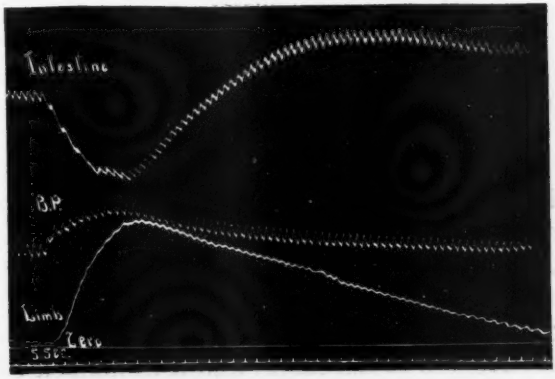

FIG. 15
Effect of a larger dose of adrenalin, 0.3 c.c., 1:10,000 in the monkey. (Reduced ⅔.)

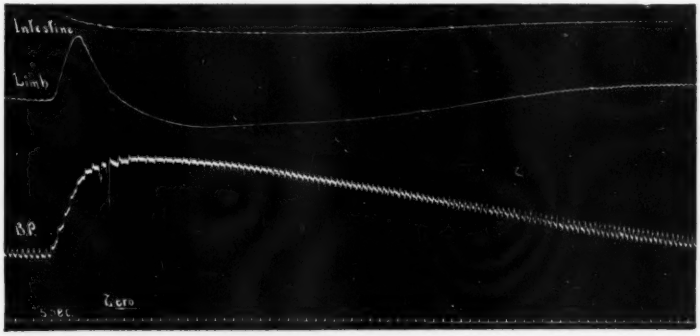

FIG. 16
Reversal in the limb produced by a large dose of adrenalin, 2.5 c.c., 1:10,000 in the monkey. (Reduced ¾.)

very well (Figs. 14 and 15) until large doses of adrenalin were used when constriction only was obtained (Fig. 16).

A fall in blood pressure was obtained from the injection of small doses of adrenalin (Fig. 13), but as sometimes happens in cats or dogs the fall became small or almost disappeared after a few doses had been injected (Fig. 14).

DISCUSSION

So far as we know the blood vessels of all vertebrates lower than mammals are constricted by adrenalin.

In the frog Burket (17) found that the constrictor effect of succeeding doses of adrenalin rapidly declines until there remains only a very small response. He also noted that the rise in pressure lasts much longer than in the cat. Our observations upon the turtle are somewhat similar, there being a rapid loss in sensitiveness to adrenalin and a prolonged effect when the rise is produced. In addition attention should be called to the fact that the threshold for a blood pressure response is much higher in the reptiles than in the mammals.

It is of interest to note also that birds resemble mammals in some respects in their behavior toward adrenalin. The threshold for adrenalin response is about as low and successive doses of adrenalin do not readily decrease the sensitiveness. The percentage rise in blood pressure that can be produced by adrenalin in the fowl is much greater than that possible in the reptile, although the rise in blood pressure is more prolonged in the fowl than in the mammal. It may be partly due to the absence of dilator mechanisms which could be affected by adrenalin and thus

tend to offset the constrictor effect. Dale (22) was able partially to paralyze the constrictor mechanism in the fowl, but he obtained no fall in blood pressure from adrenalin.

Besides the carnivores and rodents which have been extensively studied by different investigators, a few observations have been made upon the ungulates and primates. Barger and Dale (18) paralyzed the vaso-constrictor mechanism in the pig and the goat with ergotoxin, but failed to obtain a fall in blood pressure when adrenalin was injected. Barbour and Prince (19), in experiments with perfused hearts obtained dilatation of coronary vessels in the ox, sheep, pig, and rabbit, but constriction in the monkey.

Auer and Meltzer (20) obtained usually a rise, but sometimes also a fall in blood pressure from the intraspinal injection of large amounts of adrenalin in the monkey.

We have been able to show in all orders of mammals which we have studied, except the rodents, that both adrenalin vasodilator mechanisms (for skeletal muscle and intestine) are present. On the other hand, we have been unable to prove the presence of such mechanisms in the rodents. Moreover, no one else (21, 23) has ever been able to produce a fall in blood pressure by the injection of adrenalin in the rabbit. Dale (22) was unable to obtain a reversel by the use of ergot, although he abolished the pressor effect of adrenalin.

Dilatation from adrenalin had been observed in the rabbit. The Meltzers (24) obtained dilatation of the ear vessels of the rabbit from the subcutaneous injection of adrenalin. Ogawa (25) produced dilatation

of the perfused kidney, intestine and hind limbs of the rabbit by adrenalin. However, he usually obtained constriction of the kidney even with dilute solutions. He did not secure a primary dilatation in the limb. We are led to conclude as a result of our experiments that even though adrenalin vasodilatation may occur in the rabbit it is relatively unimportant.

In conclusion, we are justified in assuming that the usual vasomotor reaction in skeletal muscle is dilatation with moderate doses of adrenalin, rodents being exceptional; and because of the uniform occurrence in other mammalian orders as well as the presence in the monkey we have considerable reason for believing that these mechanisms are also present in man.

We wish to thank Lois McPhedran Fraser for assistance in a part of this research.

SUMMARY

1. Birds and reptiles possess no adrenalin vasodilator mechanisms.
2. A small amount of adrenalin produces a fall in blood pressure in marsupials, ungulates, carnivores and primates.
3. Adrenalin vasodilator mechanisms for the limb and intestine are present in marsupials, ungulates, carnivores and primates.
4. Rodents are exceptional in their reaction to adrenalin, vasodilator mechanisms sensitive to this hormone being absent.
5. Dilatation in the blood vessels of skeletal muscle is the usual response to adrenalin in mammals.

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SUPPURATION OF GOITROUS THYROID FOLLOWING ADMINISTRATION OF THYROID EXTRACT: A CASE REPORT

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The patient was a widow, aged 51 years. When first seen she was melancholic and sleepy in the daytime. She had a moderate-sized goitre. Her melancholy was increased, if not caused, by the fact that her son was in prison. A half grain dessicated thyroid after each meal was prescribed.

After a week's administration of the material the right lobe of her thyroid became painful. The treatment was stopped. After two weeks the painful lobe reddened and a week later "broke," three days after the patient, on her own volition, had applied a bread and water poultice. It may be remarked here that the mental condition cleared up rapidly after the administration of the dessicated thyroid.

On seeing her after the poulticing had been done for several days, I was alarmed at the appearance of the sloughing lobe of thyroid. I had her apply a sulpho-naphthol poultice every three hours. After a few days I snipped off the dead thyroid tissue presenting—about the size of a dime—and had her continue antiseptic treatment until healing occurred—four months later. Healing was delayed because of the necessity of the patient to do household duties.

This case illustrates the care with which thyroid extract must be given in such cases. In goitre, with myxedema symptoms, I should commence with half a

grain of dessicated thyroid a day, and watch carefully for the least sign of trouble, such as slight pain in the thyroid. On its appearance omit the medication. Enough may have been given to awaken the dormant tissue to renewed activity. If not, we can carefully renew our medication, and watch again.

A CASE OF PARATHYROID INSUFFICIENCY

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The following case is remarkable in that it is the only one which I have seen in which the symptoms appeared to be due to a functional insufficiency of the parathyroid glands; and I have not found any record elsewhere of a similar case.

Opportunity was afforded to watch this case for over four years, and the result of suitable organotherapy—the administration of dessicated parathyroid substance—was so decided that one can hardly believe that the symptoms which will be enumerated could have been produced in any other way.

Clinical History—A clerk, aged 47, came under my care late in 1910. When he was 30 years old he first noticed a slight enlargement of the thyroid gland. It gradually became larger and about two years previously—in 1908—it became necessary to remove the greater part of it. After this he remained perfectly well until four months ago, at which time quite suddenly he became greatly depressed and very nervous and restless. He suffered from an irresistible desire to keep moving, and instead of sleeping spent most of the night walking about. He began to be exceedingly tremulous and found that he had great difficulty in writing. There was a continuous fibrillary twitching of the eyelids, but no tetany was present at any time.

The general appearance was not unlike that of a severe case of Graves' disease, but his eyes were

sunken instead of being prominent and the thyroid gland could neither be seen nor felt. When he was taken ill in August (1910) he weighed 191 pounds, but now he weighed only 144 pounds, and despite an increasing appetite—he ate enormously and did not seem to suffer from this—he was losing weight rapidly.

At the time I first saw him with Sir Bertrand Dawson he complained of some difficulty in swallowing and said that the food seemed to stick in his throat. This was shown by a fluroscopic examination to be the result of irregular spasmodic contractions of the esophagus. He also had some irregular intestinal pains which might be accounted for in a similar manner. While previously he had been accustomed to open his bowels once a day, he now passed three or four large, but otherwise seemingly normal, stools each day. The urine was somewhat reduced in quantity, but otherwise normal.

He was greatly troubled with palpitation and his pulse was constantly about 120. His face and neck were deeply flushed and the secretion of the sweat glands was unaffected. It was noticed that his hair had ceased to grow, though it did not fall out and become thinner. His beard was not growing so fast and while formerly he had his hair cut about every ten days, now six weeks had passed without any noticeable increase in its length. In addition to this he had become completely impotent.

It seemed obvious that the condition was of endocrinous origin, and it was thought possible that the condition resulted from injury to the parathyroid glands during the operation on the thyroid

gland which was performed more than two years previously.

A definite diagnosis was not made and the treatment here outlined was expectant.

Treatment—He was put to bed and beside the ordinary full hospital diet, he received four pints of milk a day. His pulse gradually became slower and the abdominal discomfort disappeared. However, his weight continued to fall until it reached 130½ pounds ten days later. The restlessness was not modified and he found it extremely difficult to stay in bed. He was given large doses of opium and bromides, which had a favorable effect, and he gained slowly in weight until two months later he weighed 159 pounds. During this time desiccated thyroid gland and later Moebius's antithyroid serum were tried, but the former aggravated the symptoms and the latter made him sick.

In February though the pulse was somewhat slower and the restlessness and tremor less marked, his other symptoms were unaltered. He was allowed to get up and returned to his work.

His weight at once began to fall, and in spite of continuing the same diet and both opium and bromides, his weight on June 18th was lower than ever —127½ pounds. With difficulty he continued his work, but on that day he began to take one-tenth grain of dried ox parathyroid glands (Armour) four times daily, and four days later both the opium and the bromides were discontinued.

The gain in weight was most remarkable. During the first four days he gained 6½ pounds, the next five days 12 pounds, five pounds the next four days

and the same amount during the next six days or a total of 28½ pounds in nineteen days. Coincidently he became stronger every day, his sleep was better and more refreshing and the restlessness, tremor and dysphagia disappeared, his hair began to grow, the pulse gradually was slowed until it was less than normal, the amount of feces was reduced and the urine increased.

After a month of parathyroid therapy he was almost well, though it was not until he had been taking parathyroid gland for six months that his sexual functions were restored. About seven months after this treatment was instituted—January 11, 1912—his weight was 161 pounds and during that year he gained an additional 14 pounds; and about Christmas, 1912, he discontinued taking the parathyroid gland.

In August, 1913, he was seen again and though his weight had increased 4 pounds (it was now 179 pounds), he was more restless and his pulse was faster, so he was advised to continue to take one-tenth of a grain of the parathyroid gland daily. This was continued for four months and discontinued in November as, peculiarly enough, his face had assumed a brick red color, his throat was somewhat full and the vessels in the neck throbbed. These symptoms, however, disappeared after omitting the parathyroid.

I heard from him in February, 1914, at which time his weight was 189 pounds and he felt perfectly well and strong with no trace of nervousness, although he was working quite hard.

THE RELATION OF THE ADRENAL GLANDS TO SUGAR METABOLISM

Striking effects can be produced by the injection of adrenin. The body contains certain organs, the adrenals, capable of forming adrenin. The actual physiological function of these glands has not been satisfactorily determined. These facts have proven an irresistable stimulus to speculation and theorizing, both upon the part of clinicians and of laboratory investigators. The mysterious etiology of diabetes mellitus has been another potent stimulus to imaginative activity. Under such conditions it was inevitable that the possibility of producing glycosuria by the injection of adrenin should have led to a theory that the adrenals play an important part in sugar metabolism. The hypothesis is intrinsically attractive and has had many adherents. As usual in such cases, when the theory had been formulated a considerable amount of evidence reveals in many instances a partisan attitude,—a conscious or unconscious tendency to make the experiments support the preconceived theory. The existence of this attitude should at once awaken suspicion. To be suspicious of a given theory, however, and to disprove it are two quite different matters. Attractive theories die hard.

Many years ago Claude Bernard discovered that an irritative lesion of the floor of the fourth ventricle could give rise to glycosuria. The lesion was produced by a simple puncture through the roof of the ventricle. This is the so-called "sugar puncture" or piqure.

When the adrenal glands began to receive practical attention at the hands of investigators an attempt was made to correlate the piqure glycosuria with that produced by adrenin. Soon the literature provided the definite "proof" that, in the absence of the adrenal glands, piqure glycosuria could not be produced and that they form, therefore, an essential link in the chain of causation. Without going into a discussion of the technical details of the researches suffice it to say that the experiments cited in proof of the thesis were made upon moribund animals after severe trauma and anesthesia, all of which factors profoundly effect sugar metabolism. Under such circumstances the presence or absence of glycosuria after piqure could not logically be regarded as either proving or disproving the thesis.

Attempts to determine directly the effect of piqure on adrenal discharge were also not lacking. Kahn (1) investigated the matter at some length and concluded that no augmented discharge of adrenin took place after this operation. Later (2) he reinvestigated the problem employing more adequate technique and concluded that, as a matter of fact, the puncture does cause adrenal discharge. However, as Stewart and Rogoff (3) point out Kahn's results are not conclusive because he used a colorimetric method not suited to quantitative work or, when he used the delicate frog-perfusion method, took no note of essential conditions in the donor of the blood tested. Moreover, the quantitative factor was ignored, so far as Kahn's results were regarded as applicable to the problem of glycosuria. Osgood, working in Cannon's laboratory, has shown that to produce glycosuria it is necessary to inject many

times the maximum quantity of adrenin that can be evoked by stimulation of the nerves to the adrenals.

Following Kahn's reports a number of other papers appeared which were mostly of negative tenor and of late years the conviction has been growing that piqure glycosuria is not dependent in any essential way upon adrenal discharge. However, before negative results can be regarded as conclusive it must be shown that all essential conditions of experimental technique have been met. As Stewart and Rogoff maintain this has not hitherto been done. In particular, it must always be proven that the liver contains an adequate supply of glycogen before a failure to produce glycosuria or, what is more significant, hyperglycemia, can have any value as evidence.

The most recent investigation of the problem has been made by Stewart and Rogoff (3) in the Laboratory of Experimental Medicine at Western Reserve University. Use has been made of the fact that a considerable number of rabbits will survive the skillful extirpation of both adrenals and will afterwards have livers well filled with glycogen. A similar fact can be demonstrated for cats from which one adrenal has been removed and adrenin discharge from the other prevented by cutting its nerve supply. In such animals hyperglycemia can readily be caused by asphyxia, a fact which shows that sugar mobilization is still possible. In such animals piqure results in many cases in marked hyperglycemia. In case of the rabbit, at any rate, adrenal discharge can clearly be excluded as playing an essential part in the phenomenon and the proof in case of cats is all but absolutely conclusive. It was further shown

that, under the conditions of the experiments, injected adrenin readily caused hyperglycemia.

It may now be definitely asserted that the adrenal glands do not play any essential role in the production of piqure glycosuria and added doubt is thrown upon the theory that they play an essential part in any type of glycosuria or hyperglycemia. Whatever may be the explanation of the fact that the adrenals have an important influence upon bodily functions the burden of proof now rests heavily upon those who postulate the importance of adrenin discharge. Until this proof is forthcoming the elaborate superstructures that have been erected upon the pharmacology of adrenin have but fragile foundations. The assumption that "hypoadrenia" has any significance as an etiologic factor now needs something more substantial than mere reiteration before it is worthy of the serious consideration of intelligent clinicians.

BIBLIOGRAPHY

1. Kahn. Arch. f. d. ges. Physiol. (Bonn.) 1912, **144**, 251.
2. Kahn. Ibid, 1912, **146**, 578.
3. Stewart (G. N.) and Rogoff (J. M.) The relation of the adrenals to piqure hyperglycemia and to the glycogen content of the liver. Am. Jour. Physiol. (Balt.) 1918, **46**, 90-116.

THYROID AND THYMUS. André Crotti, M.D., F. A. C. S., LL. D. 558 pages. With ninety-six illustrations and thirty-three plates in colors. Lea and Febiger, Philadelphia, 1918.

From the general tenor of the book one gathers that the author has set out primarily to write a practical and readable book. If this was the purpose the book may be regarded as a success. The first 60 pages are devoted to the anatomy, physiology and chemistry of the thyroid gland. Of these sections that on physiology is perhaps the least satisfactory of any in the book. Two excellent chapters on pathology and inflammations occupy the next 60 pages. The next section,—the greater part of the book as a whole,—is devoted to the subject of thyroid diseases. A full discussion of classification, etiology, symptomatology and treatment of these is included. The last two chapters are devoted to the thymus gland.

A noteworthy feature of the book is the illustrating. Many of the colored plates by Marcel Guelin are beautiful examples of anatomical drawing. To a very considerable extent, however, they are superfluous for any but aesthetic reasons. Many of the points brought out could have been shown as well or better by clean cut line drawings. One can not commend the use of an expensive colored plate to illustrate so simple a matter, for instance, as the placing of a subcutaneous ligature (Plate 33.)

The book as a whole is one of outstanding excellences as well as defects. The subjects of symptomatology and treatment of goitre are especially satisfactory, as is also the discussion of the geographical distribution of endemic goitre. The treatment of the historical aspects of the goitre problem is the best with which the reviewer is familiar; a full account of the Kocher-Reverdin controversy is a case in point.

So much for the author's efforts as a practical surgeon dealing with matters of fact.

As a scientist, however, dealing with matters still open to investigation, he is less satisfactory. His attitude is indicated in the prefatory statement: "I have gathered all I consider of value from the enormous amount of French, Italian, German and English literature . . . and I have endeavored, in my recital of sources and authorities, to give credit where credit is due." One can but admire the courage of a writer assaying the role of dogmatically evaluating the literature of the difficult subject of speculative endocrinology. The author's lack of success is perhaps sufficiently indicated by a single quotation (page 333.) "We *know* that their (adrenal) cortical cells . . . are entrusted with the duty of neutralizing the muscular toxins, and that the medulary cells . . . produce adrenalin whose tonic action upon the circulatory and muscular systems is well *known*. . . . We *know,* too, that the thyroid secretion is antagonistic to that of the suprarenal bodies."* As a matter of fact none of these things is known. Such confusion of fact and theory is not uncommon throughout the book whenever the author gets outside the realm of his personal experience. He does not make sufficient distinction between the fanciful conclusions of credulous, amateur experimentalists and the critical conclusions of competent scientists. In several instances a high value is placed upon notably faulty researches. The obsolete viennese "Wechselwirkung" theories, for example, are quoted as of current worth.

The announced endeavor "to give credit where credit is due" is but poorly carried out. To a serious student the value of the book is greatly restricted by the almost constant failure to include proper bibliographic references. The few that are given are

*Italics mine. R. G. H.

mostly in slipshod form. What, with proper attention to this point might have been a valuable book of reference is, in this respect, practically useless. Neither can the attempt to "include all that is valuable" be regarded as an entire success. Several important recent papers have been missed. Among these are Bensley's and Goetsch's work on thyroid cytology, Cannon's work on the control of thyroid secretion, Marine's on iodin fixation and that of Norris on thyroid embryology.

The author's use of the English language is somewhat remarkable. Some paragraphs might be taken as models of graphic, artistic exposition, while a few might be selected to serve as models of what not to do. Colloquialisms are frequently employed. Occasional unfortunate verbal peculiarities are encountered. Some of these are: "aspirative needle," "metabolistic" for metabolic, "adipositas" for adiposity, and "catheterism" for catheterization; reference is also made to a "thyroidly insufficient patient." A lack of familiarity with English scientific idiom is betrayed by the use of such expressons as "products of refuse" for metabolites, "anorganic" for inorganic, "superficial" for *surface* tension, "albumin" for protein, "vasomotry" for vasomotor, "autonomous" for parasympathetic and "depoisoning" for detoxication.

The discussion of the etiology of goitre, and especially of Graves' disease is, as might be expected, full. The pertinent clinical evidence is skillfully assembled. The experimental evidence, however, is less satisfactorily treated. The author believes that experimental Graves' disease has been successfully produced both in man and animals by feeding thyroid substance. The only properly objective research upon the subject which is known to the reviewer, a research which McCarrison regards as the most fundamental on the goitre problem, is ignored. Carlson,

as a matter of fact, was quite unable to produce anything at all closely resembling the disease either in man or animal by thyroid feeding. The problem propounded for discussion is: "Is Graves' disease a true hyperthyroidism?" This problem is soon lost sight of, however, in the consideration of quite a different question,—namely, that of the thyrogenic origin of goitre. The final conclusion is that the malady is essentially a toxic thyroiditis. Throughout the book, as a matter of fact, "Graves' disease" and "hyperthyroidism" are used interchangably, ignoring the possibility, if not the probability, that Graves' disease is a *dysthyroidism*.

The two sections that most appeal to the reviewer are those on hypothyroidism in the young and on the water transmission of goitre. The latter is especially to be commended as a full, well-balanced exposition of the topic.

The two final chapters, on the thymus gland, have in general the same excellences and defects as those on the thyroid. The diagnosis and treatment of thymus hyperplasia are delightfully treated. In the discussion of the experimental pathology of the thymus much stress is laid on the work of Klose and Vogt,—work which various competent scientists have been unable to confirm.

Altogether it may be said that the reader who is interested in the thyroid and thymus glands from a "practical" clinical standpoint will find Cotti's book a rich storehouse of usable and entertaining lore. The reader, on the other hand, who is interested primarily as an endocrine biologist will find it unsatisfactory. To such it can be most commended for its excellent illustrations and for its historical material.

R. G. H.

80. **(ADRENAL) Disparition des enclases, lipocholestériques de la surrénale humaine dans l'agitation motrice. (Disappearance of lipoid-cholesterol bodies of the human adrenal in motor disturbance.)** Laignel-Lavastine (M.) C. R. Soc. de Biol. (Paris) 1918, **81**, 324-325.

The adrenals were examined from six cases, each of which had suffered from intense and prolonged motor disturbances before death. The author failed to find lipoid-cholesterol bodies in the adrenal cortex.—F. A. H.

81. **(ADRENAL) La teneur en cholestérine des surrénales aux différents stades de la vie foetale (Cholesterol content of the adrenals at different stages of foetal life.)** Chauffard (A.), Laroche (G.) and Grigant (A.) C. R. Soc. de Biol. (Paris), 1918, **81**, 87-89.

As the adrenals increase in size in the foetus the cholesterol content increases until at birth the average amount is 15 grams per kilogram. The cholesterol content of the liver and kidney is about 2.5 grams per kilogram at birth.—F. A. H.

82. **(ADRENAL) On the liberation of epinephrin from the ardenal glands.** Rogoff (J. M.). Jour. Lab. and Clin. Med. (St. Louis), 1918, **3**, 209.

This article is a review and critique of recent work and theories on the discharge of the adrenal secretion into the blood stream. Nothing essentially new is offered save a tentative theory that certain discharges of adrenal secretion may be due to reflexes involving a definite center located in the spinal cord.

At the close of the article the author strongly emphasizes the fact that our present knowledge of the adrenals is not sufficient to warrant epinephrectomy as a measure of relief in conditions of arterial hypertonus associated with Bright's disease, as has been done, on the assumption that this condition is associated with hyperadremia.—H. W.

83. **(ADRENAL) The relation of the adrenals to piqure hyperglycemia and to the glycogen content of the liver**

Stewart (G. N.) and Rogoff (J. M.) Am. Jour. Physiol. (Balt.) 1918, **44**, 90-116.

In rabbits which have survived the removal of both adrenals, and whose livers are well filled with glycogen, piqure causes decided hyperglycemia just as in normal rabbits. This is not compatible with the theory that piqure hyperglycemia is caused in the same way as the hyperglycemia produced by injecting adrenalin, by an increased liberation of epinephrin from the adrenals into the blood. It was frequently noticed also that hyperglycemia was caused by asphyxia in adrenalectomized rabbits.

The failure of previous observers to obtain piqure hyperglycemia in rabbits after the extirpation of both adrenals is attributed to the fact that they performed the piqure immediately after the epinephrectomy, or if an interval was allowed to elapse it was too short to permit complete recovery from the adrenal operation and the liver was insufficiently stored with glycogen. Even when a considerable interval is allowed after the adrenal operation, the state of nutrition or the diet is sometimes unfavorable for glycogen accumulation and therefore a positive result cannot be expected. There is no real evidence that piqure increases the rate of liberation from the adrenals.

It is pointed out that the reactions of denervated vascular regions and of the denervated heart, which have been interpreted as showing that the rate of liberation of epinephrin is increased by stimulation of afferent nerves and by asphyxia, may have a different significance. The response of these organs may indicate merely an increased rate of blood flow through the denervated regions and therefore an increase in the total quantity of adrenalin reaching them, without any actual change in the rate of adrenalin liberation from the suprarenal glands.

The formation and storing of glycogen in the liver is not affected by removal of both adrenals in rabbits, or by removal of one adrenal and section of the nerves of the others in cats with consequent abolition or marked reduction in the rate of liberation of epinephrin. In rats, also, extirpation of the adrenals produces no essential change in the capacity of the liver to form and store glycogen.—L. G. K.

84. (ADRENAL) Sur le fonctionnement de la capsule surrénale humaine dans les gangrénes gazeuses. (On the functioning of the human adrenal capsule in gaseous gangrene). Goormagtigh (M.) C. R. Soc. de Biol. (Paris) 1918, **81**, 14-17.

In gaseous gangrene of rapid development the adrenal cortex pours into the blood stream a large proportion of cholesterol and its ethers. Judging from the histo-chemical characteristics these substances undergo important changes at the time of passing into the blood. The elimination of cholesterol is less in sub-acute cases while in chronic cases part of the cholesterol accumulates in the center of the gland.

There appeared to be hyperactivity of the medulla.—F. A. H.

85. **(ADRENAL) Sur l'origine de la capsule surrénale chez les chéiroptéres (Upon the origin of the adrenal capsule in the chiropters).** Costa (A. C. da) C. R. Soc. de Biol. (Paris) 1918, **81**, 51-53.

Although it is generally admitted that the two portions of the adrenal have different origins, Colson thought that in chiropters the two parts had a common origin. The author attempted to verify the work of Colson, but found that chiropters agree with other vertebrates.—F. A. H.

86. **(ADRENALS) Dos casos de hematoma suparrenal. (Two cases of adrenal hematoma.)** Deluca (F. A.) Semana Médica (Bs. Aires), 1918, **25**, 93.

Two cases are discussed. The first was that of a baby who was born asphixiated but was resuscitated and appeared normal for two days. On the third day the mother noted pallor; on the fourth, jaundice developed and the infant cried all day. He was quieted by a bath but later had an attack of clonic convulsions. This was repeated several times during the night and the child died the following morning. In the second case the baby was born dead. Autopsy in each case showed hemorrhages into the adrenal glands. The parents in both cases were syphilitic. Deluca thinks that syphilis as well as extensive burns can produce the condition of adrenal hematoma.

G. P. G.

87. **(ADRENALS) Le role des Surrenales dans l'action du pneumogastrique sur le coeur.** Roger (H.) Jour. de physiol. et de path. gen. (Paris), 1917, **17**, 187.

Whereas in normal rabbits it is impossible to maintain a prolonged cessation of heart beats by stimulation of the vagus, this is possible after the suprarenals have been removed. The heart may be kept at rest so long that asphyxial convulsions occur. This state can be converted to the normal one by the in-

jection of adrenin. Accordingly, the so-called escape from the vagus inhibition is regarded as due to central stimulation of nerves to the suprarenals, probably owing to the low blood pressure.—Physiol. Abst.

88. (ADRENALS) Un caso de mal de Addison. (A case of Addison's disease.) Fonte (C.) Brazil Médico (Rio de Janeiro), 1918, **32**, 50.

Addison's disease developed in a man fifty-eight years of age,—an alcoholic; nothing of particular interest.

G. P. G.

89. (ADRENALIN) Hemmung der Kochsalzausscheidung im Harn durch Adrenaline. (The influence of adrenalin on the secretion of sodium chloride in the urine.) Frey, Bulcke and Wels. Deutsches Arch. f. klin. Med. (Leipsig) 1917, **123**, 163.

After subcutaneous injections of adrenalin the rate of excretion of sodium chloride through the kidney becomes slower. It is the same with the excretion of nitrogen. Adrenalin acts on the tissue of the kidney; in Brights' disease the reaction of the body to adrenalin is the same as in health.—J. K.

90. (ADRENALIN) L'action de l'adrenaline sur le coeur, étudiée par la radioscopie (Action of adrenalin on the heart, studied by the radioscope). Loeper (M.), Dubois (H.) and Wagner (C.) C. R. Soc. de Biol. (Paris), 1918, **81**, 85-86.

The authors studied the hearts of a large number of normal and pathological subjects by means of the radioscope before and after giving one milligram of adrenalin. The hearts of normal subjects were found to be unchanged in a majority of cases. There was dilatation in many pathological cases. This was thought to be due to the increased pressure from constriction of the arterioles and inability of the heart to recover quickly. This method is suggested as a test for cardiac defects.—F. A. H.

91. (ADRENALIN) Location of the adrenalin vasodilator mechanisms. Hartman (F. A.), Kilborn (L. G.) and Fraser (L.) Am. Jour. Physiol. (Balt.) 1918, **46**, 168-185.

Adrenalin causes vasodilatation in the skeletal muscle of the hind limb by acting on structures located in the lower lumbar and sacral sympathetic ganglia and in the dorsal root gan-

glia of the nerves supplying the limb. Similarly dilatation of the intestine is brought about by adrenalin acting on structures ganglia of the lower thoracic region. It is not probable that in the superior mesenteric ganglion and in the dorsal root the antidromic vasodilator impulses caused by adrenalin are identical with those of Bayliss since there is no evidence that the blood vessels of the skin dilate with adrenalin. These results, however, tend to support the view that the sympathetic system contains vasodilator fibers to the intestine and to he hind limb.—Authers' Abstract.

92. **(ADRENALIN) The combination of local and general anaesthetics and the use of adrenalin.** Wishart (D. J.) Can. Pract. and Rev. (Toronto) 1916, **41**, 1-4.

Includes a discussion of the use of adrenalin in local and general anaesthesia. Cites two cases in which death occurred presumably from the injection of a few drops of adrenalin solution during chloroform anaesthesia.—F. A. H.

93. **(ADRENALIN) The regulation of renal activity. IV. Regulation of urea excretion by adrenalin.** Addis (T.), Barnett (G. D.) and Shevky (A. E.) Am. Jour. Physiol. (Balt.) 1918, **46**, 39-51.

Subcutaneous injection of adrenalin in the rabbit is followed by an increased urea excretion by the kidneys. There is a certain amount of adrenalin which produces the greatest increase in function, smaller amounts having less and less effect until there is no change from the normal. With larger amounts the augmenting effect on secretion also becomes less until, with relatively large doses, the reverse effect of a decrease in function is found. Except with these large amounts the rate of urea excretion is more rapid than in animals not given adrenalin, in spite of a lowering of the blood urea concentration.

The adrenalin is supposed to influence the secretory activity of the kidney cells through the medium of something in the termination of sympathetic nerve fibers analagous to the receptive substance in the end-plates of muscle fibers.—L. G. K.

94. **(ADRENALIN) Untersuchungen über die Adrenalinwirkung auf die weiszen Blutzellen. (The effect of adrenalin on the leucocytes.)** Hatigan (J.) Wein. klin Wchnschr. 1917, **30**, 1541.

The subcutaneous injection of 0.001 gram adrenalin causes a leucotytosis. In the first hour after the injection there is a

marked increase of the lymphocytes. The second hour the lymphocytes diminish but there is an increase of the neutrophil leucocytes. It generally takes six hours before the number of leucocytes has become normal again. If a double dose of adrenalin is injected the period of lymphocytosis persists about twice the ordinary time. If atrophine or pilocarpine is previously injected the reaction to the adrenalin is not changed.—J. K.

95. (ADRENALIN, PITUITRIN) The regulation of renal activity. VI. The effect of adrenalin and pituitrin on the action of the kidney under strain. Addis (T.), Foster (M. G.) and Barnett (G. D.) Am. Jour. Physiol. (Balt.) 1918, **46**, 84-89.

The condition of "strain" was produced by giving 5 grams of urea at the beginning of the experiment.

At high blood urea concentrations the degree of change in the urea excreting activity of the rabbit's kidney produced by adrenalin and by pituitrin is less than at low blood urea concentrations.—L. G. K.

96. (ADRENIN) Action of adrenin in auriculo-ventricular dissociation. Hardoy (P. J.) and Houssay (B. A.) Revista Assoc. Méd. (Buenos Aires), 1917, **27**, 462.

In a dog with experimental dissociation and in two patients the injection of adrenin caused a different degree of acceleration of the rate of the auricles and of the ventricles. The normal rhythm was not re-established, although at a certain moment there was a false appearance of removal of the block.—B. A. H.

97. (ADRENIN) Adrenin content of the suprarenal glands of cadavers of patients dying from beriberi. Ono (S.) Jikwa Zasshi, 1916, —, 1014.

Nine acute cases of beriberi and two dying during pregnancy were examined as to the post-mortem adrenin content of the suprarenal capsules. The results of the first nine varied from 4.96 to 5.99 mgs. as compared with the normal of 2.82 mgs. and those of the fatal cases were 3.01 and 4.49 mgs. Microscopically the medullary area appeared more fatty than normal and microscopically it was thought to be the seat of a lymphatic infiltration of a mild grade.—Chem. Abst.

98. **(ADRENIN) Azione del l'adrenalina sul l'utero isolato, in riposo e gravido.** Quagliarello (G.) Arch. di Ostetricia e Ginecologia (Napoli) Serie II, vol. V, parte I. Abst. La Pediatria. April, 1918.

According to the experiments of the author the adrenalin heightens the tone in the isolated pregnant uterus, while inhibiting the virgin or the non-pregnant uterus.—G. V.

99. **(ADRENIN) Carbohydrate metabolism in the surviving dog liver.** Abelin (J.) and de Corral (J. M.) Biochem. Ztschr., 1917, **83,** 62-73. (Physiol. Abst., 2, 597.)

Perfusion of rabbit liver with a peptone solution does not affect glycogen, but in the dog it is diminished. In both animals adrenin perfusion has no effect on the hepatic glycogen.
Chem. Abst. **12,** 820.

100. **(ADRENIN) Ergotoxin and adrenin hyperglycemia.** Laurin (E.) Biochem. Ztschr., 1917, **82,** 87-95.

Stenstrom stated that the hyperglycemia and glycosuria produced by adrenin could not be prevented by injecting pituitrin. Miculicich reported the same results with ergotoxin. This remarkable similarity of action between an animal and a fungus product is confirmed. Chem. Abst. **12,** 501.

101. **(ADRENIN) Location of adrenalin vasodilator mechanism.** Hartman (F. A.). Proc. Am. Physiol. Soc., Am. Jour. Physiol. (Balt.), 1918, **45,** 555. See. Endocrin, 1918, **2,** 1.

102. **(ADRENIN) Relation between chemical constitution and physiological action.** Pyman (F. L.) Jour. Chem. Soc., 1917, **111,** 1103-28.

A lecture dealing principally with work of the past ten years on adrenin and various esters, anesthetics, etc. References are given and conclusions summarized.
Chem. Abst. **12,** 593.

103 **(ADRENIN) The combined digitalis-adrenin therapy.** Frey (W.) Deutsche med. Wchnschr. (Berlin), 1917, **43,** 872-3.

This combination method is not recommended. Chem. Abst. 12, 951.

104 ADRENIN, the effects of on the urine flow of anesthetized and unesthetized dogs. Gunning (R. E. L.). Am. Jour. Physiol. (Balt.), 1918, **45**, 528.

Adrenin in all effective dosages administered intravenously inhibits the urine flow in both anesthetized and unanesthetized dogs. The threshold of the reaction is slightly lowered in unanesthetized animals. Small injections and infusions merely decrease the flow of urine while larger doses produce a complete cessation of flow. The inhibition usually persists until shortly after the blood pressure reaction is complete. Diuresis succeeding the inhibition was not observed.

The rapid return of the flow to normal after prolonged infusions suggest that the drug exercises its inhibition on the kidney function in a way other than by the ischemia produced.

During the administration of ether the urine flow is completely checked and recovery under the anesthetic takes place slowly.—T. C. B.

105. (ADRENIN, VI) Further studies on the effect of adrenalin upon the blood flow in muscles. Gruber (C. M.). Am. Jour. Physiol. (Balt.), 1918, **45**, 302.

The present research was carried out to determine whether or not adrenalin acted centrally or peripherally in producing vasodilation in muscles.

The conclusion reached is, that "Vasodilation in muscles caused by small amounts of adrenalin is dependent upon the tonicity of the vessel wall."

Small doses of adrenalin (0.5 cc 1:100,000) bring about vasodilation by their action on the peripheral vasodilator mechanism.—T. C. B.

106. (DIABETES) Treatment of diabetes from the general practitioner's standpoint. Janney (N. W.) Jour. A. M. A. (Chgo.) 1918, **70**, 1282-87.

Of no direct endocrine interest.—R. G. H.

107. (ENDOCRINE GLANDS) Changes in the relative weights of the various parts, systems and organs of young albino rats underfed for various periods. Stewart (C. A.) Jour. Exp. Zool. (Phila.) 1918, Vol. 25.

In rats underfed from birth to 3, 6, and 10 weeks, the spinal cord, eyeballs, liver, and stomach and intestines (empty) increase considerably in weight. A less marked increase occurs

in the brain (at three weeks especially), spleen and intestinal contents (at 6 and 10 weeks, loss earlier), suprarenals and heart (progressive increase), kidneys, testes, epididymi (at 3 and 6 weeks, loss later), ovaries and hypophysis. There is no marked change in the weights of the thyroid and pineal glands, whereas the lungs and especially the thymus lose markedly. In young rats underfed for very long periods (up to 428 days), the marked increase is maintained in the weight of the spinal cord, eyeballs, suprarenals (usually), and brain (slightly). There is but slight change in the weights of the intestinal contents, kidneys, ovaries, testes(?) and pineal body. The thyroid, thymus, heart, liver (variable), spleen (variable), alimentary canal (empty) epididymi, and hypophysis (in males) usually suffer a loss.—E. R. H.

108. (ENDOCRINE GLANDS) El sistema nervioso y las glandulas endocrinas en un caso de myopathia. (The nervous system and the endocrine glands in a case of myopathy.) Navarro (J. C.) and Correas (C. A.) Soc. Med. Argent., 1917 (June 29).

Histological examination of the nervous centers, peripheral nerves, thyroid, hypophysis, suprarenals, etc., disclosed no demonstrable lesions.—B. A. H.

109. (ENDOCRINE GLANDS) Excretion of uric acid in several cases of disease of the blood glands. Nowaczynski (J.) Deutsche med. Wchnschr. (Berlin), 1916, **42,** 1478-80. (Physiol. Abst. 2, 132.)

Although purin metabolism is frequently upset in diseases of the blood glands the changes are most variable. The injection of extracts also causes varying results, though ovarin and pituitrin produce a rise in the excretion of exogenous uric acid. Chem. Abst. **12,** 941.

110. (ENDOCRINE GLANDS) The glands of internal secretion. Crispin (A. M.) La Prensa méd. Argentina (Buenos Aires) 1917, **27,** 279.

Nothing new.—B. A. H.

111. (ENDOCRINE GLANDS) The origin of progressive muscular dystrophy. Editorial, Jour. A. M. A. (Chgo.) 1918, **70,** 1376.

Discusses late work on the subject, including the possible relation of the endocrine glands to that malady.—R. G. H.

112. (ENDOCRINE GLANDS) The effect of the administration of various substances on the blood diastase of rabbits. Watanabe (C. K.) Am. Jour. Physiol. (Balto.), 1917, **45,** 30-43.

The dextrose content of the blood was increased without any change in diastase content by the administration of adrenin. Pitruitrin injections and thyroid feeding had no effect on either diastase or dextrose content.

113. (ENDOCRINE GLANDS LACTATION) Preliminary research on the effect of extracts of certain endocrine glands on the amount of milk produced by cows and goats. D'Alfonso (C.) Ind. latt. e. zootec., 1916, **14,** 215-6, 234-5, 253-4, 268-9, 286-7, 302-5, 316, 350-1; 1917, **15,** 7-9.

This is a repetition of previous studies of the effect of the injection of extracts of ovaries, testes, adrenals, thyroids, hypophysis and mammary glands on milk production.

Chem. Abst. **12,** 592.

114. (GASTRIN) Gastric secretin. Maydell (E.) Diss. Kiev, 1917. (Physiol. Abst., **2,** 415-6.)

Gastrin prepared from the mucous membrane of the pyloric part of the stomach with 0.4% HCl was injected into dogs with chronic gastric fistula and esophagotomy. A rather energetic secretion of gastric juice was obtained under such conditions; its acidity was equal to that of the juice obtained by means of sham feeding, but its digestive power was less. The immediate introduction of the gastrin into the blood acts more feebly than upon subcutaneous injection, and in the former case a decrease of blood pressure occurs, but not in the latter. If the gastrin is treated with alcohol and ether, it is possible to separate two component parts, one of which evokes secretion and the other dilates blood vessels. Gastrin is absorbed neither by the duodenum nor by the large or small intestine. The gastrin prepared from the fundic region is inactive. Atropine diminishes the secretory effect of gastrin.

Chem. Ast. **12,** 718.

115. GLAND EXTRACTS, the bacteriolytic action of, on tubercle bacilli. Porter (A. E.) J. Hygiene (Lond.), 1917, **16,** 55-65.

The results obtained point to a consistent relationship between lipolytic activity and bacteriolytic power on tubercle

bacilli. The least bactericidal extract was lung extract and the most powerful was pancreatic extract. Liver, thymus and lymphatic glands were strongly bactericidal. Other organs, suprarenal glands, pig and cat spleen, human and cat kidney, human and ox brain, ox thyroid, cat lung, ox bone marrow, and ox pituitary glands were found to be bactericidal to a lesser degree. Human skin extract was fatty and cloudy in appearance and exceptionally rich in esterases. This sample of skin bears out the relationship between lipolysis and bacteriolysis of tubercle bacilli in a striking way, as it was extremely bactericidal. No difference was observed between human and bovine tubercle bacilli in susceptibility to any gland extract examined. Other acid-fast bacilli, though on the whole less susceptible to the influence of these extracts, were bacteriolyzed by them. They were also killed by one lung extract (pig) which contained an unusual amount of olein lipase and which had no effect on tubercle bacilli.—Chem. Abst.

116. (GONADS) Körpertemperatur und Pubertätsdrüsen. (Bodily temperature and the sex glands.) Lipschütz (A.) Arch. f. d. ges. Physiol. (Pflüger's) (Bonn) 1917, **168,** 177.

The temperature of female animals is about 0.6-0.7° C. higher than that of males. After castration the temperature becomes about 0.4° lower. When after this operation a testicle is implanted the temperature becomes still lower.

In male animals, however, castration has no influence on temperature. When after castration an ovary is implanted the temperature rises until it reaches that of normal female animals.—J. K.

117. (GONADS) Microrchidie et gynecomastie consécutives á une orchite double. Laignel-Lavastine (M.) and Courbon (P.) Presse Méd. (Paris) 1917, **25,** 492.

Before the Société Medicale des Hopitaux (July 20, 1917) the case of a soldier of 22 was presented, who after suffering from mumps last December, which was complicated by a double orchitis, began to present retrogressive evolution in the reproductive organs. Virility was lost and there was a remarkable transformation of the secondary sex characteristics and the establishment of those of the opposite sex. Little by little these changes were accentuated and the mammae attained a marked degree of hypertrophy with atrophy of the testes and penis. The authors consider this of the plastic type of hermaphroditism.—H. R. H.

118. (GONADS) Spontane Geschlechtswandlung beim Hunde in Verbindung mit Morbus Basedowii. (Spontaneous change of sexuality in a dog suffering from Graves' disease.) Heilborn. Deutsche med Wchnschr. (Berlin) 1918, **44**, 213.

A very remarkable case is described. A male dog becomes very nervous and thin and shows an exophthalmos; there is a large goitre and tachycardia; in the last two years the testes have become atrophic and the mammary glands larger. The most typical symptom, however, was an absolute homosexuality. The author does not discuss whether the changes in the thyroid have anything to do with the homosexuality.—J. K.

119. (GONADS) The effects of inanition upon the development of the germ glands and germ cells of frog larvae. Swingle (W. W.) Jour. Exp. Zool. (Phila.) 1918, Vol. 24.

Immature frog larvae were starved from the time of their emergence from the egg capsule for over one hundred days. During this interval the tadpoles were fed a few filaments of algae at odd times to prolong the experiment. No growth occurred, nor were there any indications of metamorphic changes. The control animals developed normally and underwent metamorphosis at the usual time. Microscopic examination of the gonads and germ cells showed that in the starved animals growth and development of these structures had, like somatic development, been completely inhibited. In one or two of the oldest animals of the starved series, germ cells were observed which appeared to be in the early maturation stages.

Drawings and photographs are given illustrating these points.—E. R. H.

120. (GONADS) Vorherbestimung der Geschlechts. (Is it possible to prophesy the sex of the child during pregnancy?) Konigstein (R.) Zentralbl f. Gyn. (Leipsig) 1917, **41**, 1097.

Theoretically it would be quite logical when if the child in pregnancy is a boy, the serum of the mother would contain "protective ferments" against testicle. The experiments by Konigstein in this direction gave from time to time a positive result, but not regularly enough to be of clinical value. The results, however, were remarkably better when, instead of ordinary testicle, that of an embryo or a calf was used.

121. (HYPOPHYSIS ADRENAL) The relation of the glands of internal secretion to milk production. Hammond (J.) and Hawk (J. C.) Jour. Agr. Sci., 1917, **8**, 147-53.

The flow of milk produced by an injection of pituitary extract varies with the state of nutrition of the injected animal. The ratio of morning yield to pituitary yield rises with the fall of nutrition and falls as the nutrition rises again. Therefore the yield obtained as a result of pituitary injections tends to be more constant than the morning or daily yield. The fat percentage of the pituitary milk is increased by the state of lowered nutrition in the same way as with normal milk. Injections of adrenin give results similar to those of pituitary extract in causing hyperglycemia, but different in having no immediate action on milk secretion. The secondary effect on milk secretion is a decrease in the amount of milk produced for a period of a day following the injection. The fat percentage in the milk from the period following an adrenin injection is above normal but the absolute amount obtained is decreased. The rate of blood flow is very susceptible to changes in the sugar metabolism of the animal. Chem. Abst. **12,** 822.

122. (HYPOPHYSIS) Acromegaly. Castex (M. R.) La Presna méd. Argentina (Buenos Aires), 1918, Supplement 25 (Feb. 10).

Although the subject (evidently acromegalic) presented an appearance of the sella turcica on the X-ray plate of an advanced stage of the disease and showed certain visual disturbances, the author believes that the symptoms, even headache and vomiting, are due to syphilis. He thinks the symptoms could all be ascribed to a functional defect of the pituitary secretion and doubts the existence of a tumor.—B. A. H.

123. (HYPOPHYSIS) Cirurgia da hypophyse. (Surgery of the hypophysis.) Novaes (J.) Brazil Médico (Rio de Janeiro), 1917, **31,** 431.

Novaes in a review of an article by Segura criticises the latter for leaving the accessory hypophysis. G. P. G.

124. (HYPOPHYSIS) Control of polyuria in a case of diabetes insipidus by means of hypophyseal extract. Rosenbloom (J.) Jour. A. M. A. (Chgo.), 1918, **70,** 1292.

The case of a boy of 12½ years is described in which polyuria of 9 years' duration existed. Thyroid tablets, 6 grains a day, were without effect, as were also pituitary tablets. Pituitary solution, however, injected subcutaneously brought about an almost three-fold reduction of the urine. The effect lasted about 24 hours.—R. G. H.

125. (HYPOPHYSIS) Beiträge zur Pathologie der Hypophyse. (Pathology of the hypophysis.) Fahr (T.) Deutsche Med. Wchnschr. (Berlin) 1918, **44**, 206.

A woman of 50 years suffered from convulsions; the Argyll-Robertson symptom was positive; the Wassermann reaction negative; the blood pressure was normal and the skin showed a brown pigmentation as in Addison's disease. The postmorten examination showed atrophy of both suprarenal bodies; medulla and cortex were both affected. Macroscopically the pituitary body showed no changes; microscopically, however, nearly the whole organ was changed to a mass of connective tissues, except the pars posterior, which showed no pathological changes.—J. K.

126. (HYPOPHYSIS) Further studies upon amphibian larvae from which the anterior lobe of the hypophysis had been removed. Allen (B. M.) Anat. Rec. (Phila.) 1918, Vol. 14.

The anterior lobe of the hypophysis was removed from larvae of Rana pipiens and Bufo lentiginosus as described in an earlier paper. The observations previously published were verified and much extended because of greater success in rearing the operated tadpoles. Several are still alive.

Limb development in both species is greatly retarded, running parallel with the condition in tadpoles from which the thyroid gland has been extirpated. In Bufo there is a color change to a light yellow-brown, and contrary to the case in Rana there is little retardation of bodily growth. The pars nervosa of the hypophysis forms normally in tadpoles, both Rana and Bufo, from which the anlage of the anterior lobe has been removed. There is, of course, no pars intermedia formed.

Gonads of operated Rana tadpoles were compared with normal controls of the same size killed several months before. They showed the same features as to size, structure, and germ-cell development as seen in the controls. The same correspondence in the gonads was noted when comparison was made with some small thyroidless tadpoles of the same size killed at the same time.

The retardation of bodily growth in Rana prevented the gonads from reaching the size attained in the controls at metamorphosis three months before. In Bufo, however, the operated tadpoles reached a bulk double that at metamorphosis. Correspondingly, the gonads and germ cells developed far beyond the condition attained at the time of metamorphosis in the controls.—E. R. H.

127. (HYPOPHYSIS) Pituitary disturbance in its relation to the psychoses of adolescence. (Abstract.) Tucker (B. R.)

A general description of the functions of the pituitary gland and of its anterior and posterior lobes is given.

Remarks are made upon the period of adolescence and the physiological disturbances of the pituitary secretion occurring at this time. The pathological disturbances of the pituitary secretion causing the psychoses are then taken up.

Pituitary adolescent psychoses are divided into four groups:

1st—Those with a pre-adolescent history of hypersecretion, in which during adolescence the secretion is apparently still further increased;

2nd—Those in which there is a history of pre-adolescent hypersecretion, in which during adolescence this secretion is markedly diminished;

3-a—Apparently normal pre-adolescent cases in which the secretion during adolescence is increased.

3-b—Those with an approximately normal pre-adolescent pituitary history, in which during adolescence the secretion is diminished;

4th—Those cases with a history of pre-adolescent decreased secretion, in which during adolescence the secretion is apparently still further decreased.

Cases are cited with radiographic findings to illustrate these groups and a description of their psychoses given.

Author's abstract. Read before neurological section, American Medical Association, Chicago, June, 1918.

128. (HYPOPHYSIS) Poliuria no hipofisiaria en un cancer de la mama con metastasis. (Non-hypophyseal polyuria in mammary cancer with metastasis.) Houssay (B. A.) Reunion de Médicos del Hospital Alvear, 1917 (June 29).

The author remarked that according to his experimental studies the so-called hypophyseal polyuria does not depend upon the hypophysis. In a clinical case studied a polyuria of 3-4 litres was not influenced by injections of pituitary material. At autopsy metastases were found in the frontal and bacilar sinuses and in the meninges, but the hypophysis and adjacent cerebral zone were not affected.—B. A. H.

129. (HYPOPHYSIS) Sobre o tratamento dos tumores da hypophyse e, especialmente, da acromegalia. (Treatment of hypophyseal tumors and especially of acromegaly.) De

Castro (A.), Souza (O. de) and Novaes (J.) Brazil Médico (Rio de Janeiro), 1917, **31**, 415.

De Castro reviewed favorably the work of Segura, who was the first in South America to undertake the surgical treatment of pituitary tumors. Souza agreed with de Castro that attention should be paid to the parahypophysis. Novaes reviewed the Austrian statistics and concluded that both the nasal and frontal approaches to the hypophysis are very dangerous. G. P. G.

130. (HYPOPHYSIS) Sobre un caso de poliuria esencial, de aparición a los 3 años de dad. (A case of polyuria appearing at the age of three.) Deluca (F. A.) Semana Médica (Bs. Aires), 1918, **25**, 422.

Deluca discusses the theories of polyuria including the hypophyseal variety. He reviews the experimental work of Camus and Roussy and of the Houssay, which indicates that the condition is produced by injuries of a certain basal zone rather than of the gland proper. (See Houssay, Endocrin., 1918, **2**, 94.) A complete review of the Argentine literature on the subject is included. A case is discussed of a boy three years of age who complained of marked thirst and who passed four litres of urine daily. A detailed study of the case was not permitted. G. P. G.

131. (HYPOPHYSIS) Su un infermo con sindrome psichica e femminilismo hipofisario, guarito con l'asportazione di vegetazioni adenoidi. Caliceti (P.) La Pediatria (Napoli) 1918, **26**, 233.

The author refers to one of three cases of hypophyseal feminism with psychic syndrome, caused by adenoids, according to Prof. Citelli's opinion and his own. The patient has been seen eight months after the removal of the adenoids and showed a wonderful change from his previous conditions.

Physically stronger, with a much better color, lively and quick, he was not showing dullness or apathy as before. His hair on the face and on the pubis is now practically normal; and the sleep as well as his psychic behavior do not now longer show any abnormality.

Such an effect hardly eight months after the removal of the adenoids points—1st, to the hypophyseal nature of his previous feminism, asthenia and psychic syndrome; 2nd, to the right surmise of Prof. Citelli, that the adenoids may be the *cause* and not the effect (according to Poppi's theory) of hypopsyseal alterations; 3rd, to the efficacy of intervention, even

late, whenever the hypophyseal alterations are not grossly anatomical.—G. V.

132. (HYPOPHYSIS) The action of hypophysis extracts on gastric juice secretion and gland secretions in general. Pal (J.) Deutsche med. Wchnschr. (Berlin), 1916, **42**, 1030.

This paper concerns the action of the extract of the infundibular portion of the hypophysis on gastric secretion, on the action of the kidneys and other exocrine glands, as well as on the thyroid. In summary, the extracts act inhibitingly on certain glands. This action is demonstrable in man in cases of hypersecretion (on the kidneys in diabetes insipidus, on the thyroid in hyperthyroidism, and on the stomach mucosa in hyperacidity). On the other hand, it promotes the secretion of the mammary gland and the excretion into the follicles of the thyroid, but only when there is hyperfunction of these glands. The secretion of the innervated glandular apparatus (stomach glands, kidneys, etc.) is not only dependent on the irritability of the secretory nerves, but also of the inhibitory nerves. The depressant action of the infundibular extract on the secretion depends on the action of the extract on the irritability of these nerves, which are located in the sympathetic. The stimulating action can be traced to a direct action on the cells.—Chem. Abst.

133. (HYPOPHYSIS) The arterial supply of the human hypophysis. Anat. Rec. (Phila.) 1918, Vol. 14.

Three methods are being used: (a) Injection with thin celloidin and corrosion by artificial gastric juice—somewhat unsatisfactory because of difficulty of injecting finer vessels, and because relations of arteries to tissues are not preserved; (b) wax reconstructions of thick colloidin sections of foetal specimens—sections not yet studied; (c) dissection under binocular of gelatin-injected vessels.

Brains for dissection are injected through the common carotid, with contra-lateral carotid, both vertebrals and external and internal jugular veins ligatured. Robin's Prussian blue and carmin have been used. The base of the brain in the region of the sella tursica and the underlying bone are removed and preserved in formalin. The brain and meninges are carefully freed from the underlying bone, dehydrated and cleared in cedar oil. They may then best be dissected under oil of wintergreen with a binocular.

The brains are dissected through their underlying meninges successively upon two planes: (1) an intradural

plane, comprising the internal carotids and their branches within the cavernous sinus; (2) a subdural plane comprising the circle of Willis and its branches. Four brains only in the intradural plane have thus far been dissected.

In each of these four brains there are found, arising from each internal carotid at its first and superiorly convex flexure in the cavernous sinus, an artery of approximately one to two millimeters in diameter which quickly breaks up into several somewhat variable branches. These branches, together with an inconstant artery which may arise from the carotid in the sinus cavernosus more anteriorly, supply the semilunar ganglion, the third, fourth, fifth and sixth nerves in this region and the contiguous dura mater. One of the branches on each side, ramifying, courses between the layers of the dura across the posterior lobe; twigs are sent also to the dura and may even be sent to the anterior lobe.

The branch described is probably sufficient to supply the posterior lobe, but apparently does not form a considerable element in the supply of the highly vascular anterior lobe.—E. R. H.

134. (HYPOPHYSIS) The development of the pars tuberalis of the rabbit's hypophysis. Atwell (W. J.) Anat. Rec. (Phila.) 1918, Vol. 14.

For the rabbit it has been possible to trace the development of the paired anlagen of the pars tuberalis of the hypophysis from an earlier stage than that given by Tilney ('13) for the chick and the cat, or by Miller ('16) for the pig. From the thickened epithelium which early lies in front of Rathke's pocket two thickened ridges are developed. These ridge-like eminences may be called the latral lobes, and are evident in embryos of 10 days. At 14 days these lobes have begun to grow out laterally and are more sharply constricted from the body of the hypophysis.

The lateral lobes are the anlagen of the pars tuberalis of the adult hypophysis. They begin to be in relation with the brain wall at 16 days of development, and by 19 days a considerable portion lies spread out under the diencephalic floor. There are present at this stage two blunt nasal horns extending toward the optic chiasm and two sharper caudal horns extending backward to surround the neck of the neural lobe. The caudal horns have completely surrounded the infundibulum, and have met in the mid-line by the end of the twenty-eighth day. The nasal horns fuse with each other a day or so later.

Since the lateral lobes of the mammalian hypophysis may be seen early in development, it is now easier to consider them

homologous with the lateral lobes of the reptilian hypophysis.

Because of its paired origin, the anterior part of the pars tuberalis cannot be homologized with the "Vorraum" of the reptiles, as is done by Woerdeman ('14).—E. R. H.

135. (HYPOPHYSIS) Trastornos hipofisiarios en Ginecologia. (Hypophyseal disorders in gynecology.) Guardado (J.) Revista de la Asociacion Medica Argentina (Buenos Aires) 1918, p. 256, (March).

Certain cases of amenorrhea in which ovarian opotherapy had been unsuccessful were treated with posterior lobe pituitary extract with favorable results. In other cases the treatment failed. The author thinks that the pituitary extract stimulated the ovaries.—B. A. H.

136. (HYPOPHYSIS) Veränderung in der Hypophysis cerebri bei Kretinismus und Myxoedem. (Changes in the pituitary body in cretinism and myxodema). Eichhorst. Deutsches Arch. f. klin. Med. (Leipzig) 1916, **124**, 207.

In cretinism and myxodema a hyperfunction of the pituitary body is observed. The organ becomes larger and shows an enormous hyperemia. Often hemorrhages are observed. The glandular cells grow; the chromophil cells degenerate and are replaced by cells which show the same structure as the pregnancy cells of Erdheim and Stumme. Later on a growth of the connective tissue is to be seen; then the glandular tissue becomes atrophic; in the connective tissue necrosis and the formation of cysts is observed. At the end of the disease the pituitary body becomes smaller and smaller.—J. K.

137. (HYPOPHYSIS-SYMPATHETIC SYSTEM) Diabetes insipidus in pregnancy. Novak (J.) Berlin. klin. Wchnschr. (Berlin), 1917, **54**, 107-9.

This condition is due to stimulation of the sympathetic system. A study of cases in which the hypophysis enlarges in pregnancy shows that the regulating centre is not altogether in the bulb but partly in the mid-brain. Chem. Abst. **12**, 914.

138. (INTERNAL SECRETION) Adiposis dolorosa Dercumsche Krankheit mit Beteiligung der optischen Leitungsbahnen. (Dercum's disease with ocular symptoms.) Behr. (C.) Klin Monatsbl. f. Augenheilk. (Berlin) 1917, **59**, No. 728.

A case of adiposis dolorosa with amblyopia was treated with thyroidine without success. Pituitary extract ("Hypophysin") raised the vision to 7/15.—J. K.

139. (INTERNAL SECRETION) Is the course of experimental cramp modified by disturbance of the internal secretions? Fischer (J.) Sitz. nat. Ges. Rostock, 1914, **6**, 1-2.

Fischer believes that the course of experimental cramp is modified by disturbances of the internal secretions. The absence of the thyroid and epithelium increases the cramp-producing component of the amyl nitrate action, while the absence of the suprarenals decreases it.—Chem. Abst.

140. INTERNAL SECRETIONS. Collip (J. B.) J. Can. Med. Assn. (Toronto), 1916, **6**, 1063-1069.

Nothing new.—F. A. H.

141. (INTERNAL SECRETIONS) Lidodystrophia Progressiva in a male. Weber (F. P.), Brit. J. Chil. Dis. (Lond.) 1917, **14**, 179.

The author presents a table of all of the cases of this condition in males reported in the literature, and describes a case in a boy of 13 years. This boy was moderately fat in the face and body until the age of 8 years. He then began to look thinner in the face, although in all other respects he continued to appear and feel perfectly well. The loss of fat gradually progressed and for the last three years there has been practically no fat left on the face and neck, except in the orbits. The fat covering on the gluteal regions and on the lower extremities, however, is fairly normal.—M. B. G.

142. (INTERNAL SECRETIONS) Results observed in a further study of prenatal causes of dentofacial deformities. Weinberger (B. W.) Dental Items of Interest, 1918, **40**, 6-31.

A discussion of the factors influencing the growth of the bones of the face and the teeth, with special stress on the role of the internal secretions. Chem. Abst. **12**, 933.

143. (INTERNAL SECRETIONS) Sexual precocity in the male. Strauch (A.) Amer. J. Dis. Chil. (Chgo.) 1918, **15**, 132.

The author makes an exhaustive study of the literature on this subject, quoting freely from several sources and attempts to sum up our present knowledge of the condition. In a few

observations premature sexual development has been ascribed to such early and excessive practices as masturbation and cohabitation due to seduction. Where such pathological factors are absent, what may be the cause of the prematurity of the impulses for the somatic changes remains a problem. Though the nature of the primary stimuli that control these changes is not known, it is established that the endocrine glands in their interlocked and mutually affecting functions are of the greatest importance for the normal growth of the body and for sexual maturity, among them especially the genital glands, the adrenals, the pituitary body, the thyroid and the so-called "puberty glands," the thymus and the pineal.

The author quotes several cases in the literature in which the etiological factor was a tumor of the generative glands. He thinks that these tumors suggest that the irritation of the gonads causes an excessive and premature increase of the function of the interstitial tissue of Leydig, hastening the development of the secondary sexual characteristics. Where the causes were tumors of the adrenals, he ascribes to these merely a hastening influence on the development of the secondary sexual characteristics, causing also an excessive growth of the body, since other recognizable sexual functions, such as menstruation or ejaculation, are not mentioned in the reported cases. The relation between genital hypertrophy and the pineal gland is perhaps to be interpreted as due to a premature decrease of the functionating glandular tissue, which otherwise under normal conditions undergoes degeneration, beginning with the seventh year of life. The trophic disturbances, that is, the premature development, may be considered as a manifestation of the insufficiency of the epiphyseal gland.—M. B. G.

144. (INTERNAL SECRETIONS) Studies of internal secretions in their relation to the development and condition of the teeth. V. Summary of miscellaneous findings. Gies (W. J.) Dental Cosmos, 1917, **59**, 1238.

Thyro-parathyroidectomy has no influence on the dentition of young white rats. Parathyroidectomy, without material disturbance of the thyroid, almost invariably produces deficient calcification, but has no influence on the general conditions or dimensions of the teeth. "Possibly the thyroids normally tend to induce deficient (subnormal) calcification of the teeth and the parathyroids normally tend to induce correspondingly excessive (supernormal) dental calcification." Physiological variation in the composition of the teeth, in rats, is relatively slight. Chemical changes in developing enamel occur under the influence of substances that originate outside of, and enter

or superficially affect, the cells involved in the production of enamel.—Chem. Abst.

145. LYPODYSTROPHIA PROGRESSIVA. Spear (I. J.). Arch. Int. Med. (Chgo.), 1918, **21,** 39.

Case report of lypodystrophia progressiva occurring in a school girl 15 years of age who otherwise showed no pathological findings. The case has progressed continuously for the past six years. Thyroid extract failed to retard the progress of the disease. The author does not accept the view that the condition is due to abnormal function of the endocrine glands, but considers it closely related to the muscular dystrophies; one factor having to do with dystrophy of fatty tissue, the other with muscular tissues. There were no indications of altered functioning of the ductless glands.—H. W.

146. (MENSTRUATION) Sindroma apendicular en la menstruación. (Appendiceal symptoms in menstruation.) Platero (H.) Rev. Méd. del Uruguay (Montevideo), 1918, **21,** 71.

Three cases are described in which virgins without evidence of genital injury or infection had pain at McBurney's point for three or four days preceding menstruation. At operation swelling of both appendix and ovaries was noted. In one case pus was found in the peritoneal cavity. G. P. G.

147. MONGOLISM associated with congenital cataract. Weber (F. P.) Brit. J. Chil. Dis. (Lond.) 1917, **14,** 267.

According to Weber, the only other published case of association of mongolism with congenital cataract was that of W. B. Hill, reported a few years ago.

The author reports a case of a boy of 13 months with a typical mongolian facies, protruding tongue, rhacitis, and congenital cataract. The thumbs and little fingers were rather short in proportion to the other fingers, the little fingers presented a slight lateral curvature with the concavity of the curve toward the other finger.

The mother of the boy gave a negative Wasserman reaction.—M. B. G.

148. (MONGOLISM) Congenital heart disease in a mentally defective child with a negroid-mongoloid facies. Weber (F. P.) Brit. J. Chil. Dis. (Lond.) 1917, **14,** 269.

The author reports a case of a girl of 4 years with a brachycephalic head, upward slant of palpebral fissure, broad nose with low flat bridge, lips and cheek and soft parts above eyes thick and coarse, hair scant and curly, no hair on eyebrows, no lower and hardly any upper eyelashes. The face was highly colored at times. The thyroid could be felt but was not enlarged. There was dry skin and xeroderma, but no signs of rickets. The heart showed a definite systolic murmur, was always present, especially well marked over the base to the left of the sternum (perhaps a congenital pulmonary stenosis); X-ray examination showed a shadow on that side. The Wassermann reaction of the mother was negative. W. B. Hill has stated that 10 to 20 per cent of all cases of Mongolian type have congenital heart disease.—M. B. G.

149. (MUSCULAR DYSTROPHY) Chemical changes in the blood and urine in progressive muscular dystrophy, progressive muscular atrophy and myasthenia gravis. McCrudden (F. H.), Sargent (C. S.). Arch. Int. Med., 1918, **21**, 252.

In three cases of progressive muscular dystrophy were found muscular weakness, hypoglycemia, hypocholesterinemia, creatinuria and normal excretion of ammonia. Treated patients demonstrated a rise in blood sugar with a parallel increase in strength.

Blood sugar was found low in one case each of progressive muscular dystrophy and myasthenia gravis and normal in progressive muscular atrophy. Creatinuria was present in the cases of progressive muscular atrophy and dystrophy and absent in myasthenia gravis.—H. W.

150. MUSCULAR DYSTROPHY, the endocrine origin of. Janney (N. W.) and Goodhart (S. P.). Arch. Int. Med. (Chgo.), 1918, **21**, 189.

The authors discuss the clinical and laboratory findings in a representative series of cases (9) of muscular dystrophy in children and adults. Metabolism experiments on these cases gave the following results: marked decrease in preformed creatinin in the urine; abnormal presence of creatin in the urine; low percentage of creatinin in the blood; normal amounts of creatin in the blood; hypoglycemia; delayed utilization of glucose. Distinct osseous changes accompany muscular dystrophy in most cases which resemble closely those conditions found in cases of disturbed function of the organs of internal secretion. Other changes indicative of general endocrine disturbance found in these cases were dryness and abnormal

pigmentation of the skin, brittleness of the hair, hypertrichosis, trophic changes in the nails, unusual distribution of fat and both hypertrophy and underdevelopment of the genitalia. Retardation of growth, a symptom indicative of endocrine hypofunction, was characteristic also of several of these cases.

After an extensive comparison of conditions found in muscular dystrophy with altered endocrine function the authors point out the possibility of muscular dystrophy and perhaps other so-called myopathies being in reality nothing more than symptom complexes caused by deficient function, not of one, but of various endocrine organs affected separately or coincidently.

This attitude appears reasonable in view of the fact that the symptoms which are known to represent dysfunction of one ductless gland are often very similar to or identical with manifestations of the affection of another. For instance, stoppage of growth, adiposity and defective bone formation are known to result from lesions of either the pituitary, the thyroid or the sex glands. Hence, if these symptoms are associated with such widely different organs, it seems probable that muscular dystrophy may likewise represent a symptom complex which may be caused by dysfunction of various ductless glands singly or collectively. Therefore, muscular dystrophy cannot be ascribed to hypothyroidism, as the results of former investigations might seem to indicate. The fact that the hypophysis was unquestionably affected in one case and possibly the pineal body in two others, illustrates how difficult it would be to explain the present series of cases on a basis of hypothyroidism or disturbances of the hypophysis.—H. W.

151. MUSCULAR DYSTROPHY, progressive. McCrudden (F. H.) Jour. A. M. A. (Chgo.) 1918, **70**, 1216.

"In progressive muscular dystrophy, we find low blood sugar, and, following treatment which increases the blood sugar, an improvement in muscular strength.

"Blood sugar is the source of energy for muscular contraction. Active muscle rapidly uses up glucose. As the supply becomes exhausted, muscular strength diminishes and can be restored only by glucose. Agencies such as Addison's disease, diphtheria toxin, and phosphorus and hydrazin poisoning, which reduce the blood sugar, cause profound myasthenia, the severity of which is proportional to the fall in blood sugar. Hypoglycemia, then, sufficiently accounts for the myasthenia, the most striking symptom of progressive muscular dystrophy.

"As the glucose of the blood is used up by the muscles, the loss is rapidly and quantitatively made good from the store of

glycogen in the liver, the blood sugar being thereby maintained at a fixed level. Hypoglycemia can result only from a failure of replenishment to keep pace with the needs, that is, from a loss of balance between supply and demand. Greater needs, such as increased utilization of sugar, or loss through the kidneys, can be ruled out in progressive muscular dystrophy. There is no rise in heat formation such as would accompany increased sugar catabolism, and the urine is free from sugar. A rapid fall in blood sugar during the first twenty-four hours of starvation—in health, the normal blood sugar level is maintained during starvation—testifies that in progressive muscular dystrophy, as in all forms of experimental hypoglycemia, there is a decreased rate of replenishment resulting from a diminished reserve of glycogen.

"The diminished glycogen reserve in experimental hypoglycemia results from impaired glycogen formation. The carbohydrate ingested is not converted into glycogen, but remains a long time in the blood, after which it is probably changed to fat. The deposition of fat in the muscles points to a similar impairment of glycogenesis in progressive muscular dystrophy.

"Impaired glycogenesis may result from damage either to the liver or to the suprarenals, the organs that control the process or other endocrine glands. If the fault is with the suprarenals, administration of epinephrin restores normal glycogenesis. If the fault is with the liver, epinephrin has no effect. A prompt and marked rise in blood sugar following the administration of epinephrin in progressive muscular dystrophy testifies to the efficiency of the liver in this disease and points to a deficiency in epinephrin."—Abbreviated from original.

152. (OVARIES) Hernias conjenitas tubo-ovaricas. (Congenital tubo-ovarian hernia.) Lugones (C.) Soc. Med. Argent., 1917 (June 29).

Among fifteen cases observed in little girls there were two in which the ovaries were removed on account of hermorrhagic cysts. Microscopic examination confirmed the presence of hermorrhagic cystic cavities.—B. A. H.

153. (OVARY) Effect of hysterectomy on ovarian function. Richardson (E. H.) Proc. Am. Gyn. Soc., Jour. A. M. A. (Chgo.) 1918, **70,** 1885.

"The uterus is not essential to a continuation of ovarian function, except as regards menstruation and reproduction. The disturbances of ovarian function attributed to hysterec-

tomy are partly those associated with normal menstruation and partly those arising from damage to the ovary through operative trauma or disease. The weight of evidence furnished by anatomic, experimental and clinical investigations is overwhelmingly in favor of retention of sound ovaries both before and after the menopause age."

154. (OVARY) End results of the conserved ovary. Polak (J. O.) Proc. Am. Gyn. Soc., Jour. A. M. A. (Chgo.) 1918, **70**, 1975.

"From a study of seventy-three reoperations on patients in whom one or both ovaries were conserved, we must draw the following conclusions: 1. Routine conservation without due consideration of the ovarian and contiguous pathologic condition as it exists in the individual case, is not good teaching. 2. Regeneration of the conserved ovary depends largely on the type and duration of the existing infection and the condition of the tunica of the individual ovary. 3. Even when the most detailed technic is observed, the ovarian circulation is impaired. 4. The retained ovary, without the uterus, is always a focus for possible trouble. 5. The life history of the retained ovary is of short duration, and the trophic influence of the diseased ovary has been overestimated. Finally, a cured patient has few nervous symptoms."

155. (OVARIES) Evidence of toxic action of ovaries of Gar. Greene (C. W.), Nelson (E. W.) and Baskett (E. D.). Proc. Am. Physiol. Soc., Am. Jour. Physiol. (Balt.), 1918, **45**, 558.

156. (OVARY) La función endocrinica del ovario y la secreción mamaria. (The endocrine function of the ovary and mammary secretion.) Coni Bazan (F. A.) Semana Médica (Bs. Aires), 1918, **25**, 570.

In 1915 Coni Bazan published with Berutti an article upon mammary deficiency in lactating women treated with ovarian opotherapy, corroborating various observations first recorded by Goñalons in 1914. The latter reported the successful use of corpus luteum in the treatment of these cases, adducing numerous clinical and experimental observations. Goñalons has discussed the matter also in a paper in Surg. Gyn. and Obst.

In his earlier article Coni Bazan stated that all cases of mammary insufficiency are preceded by menstrual disorders of hypovarian origin. The later paper is based upon a more careful study of cases in which corpus luteum or ovarian treatment influenced favorably the scanty milk secretion. As the

latter condition improved other symptoms of ovarian deficiency decreased. It is stated that these cases, called by pediatricians "essential hypogalactia" are actually hypovarian hypogalactia.
G. P. G.

157. (OVARY) Oogenesis in the white mouse. Kingery (H. M.), Jour. Morph. (Phila.) 1917. Vol. 30.

In the development of the ovary of the mouse there are two proliferations of cells from the germinal epithelium. The first, occurring before birth, gives rise to "primitive germ cells" and their follicle cells; the second, extending from about birth, or a few days after nearly to sexual maturity, forms the "definite ova" and their follicle cells. The primitive oocytes undergo synizesis (contraction of the chromatin) and then pass through the stages pachytene, diplotene, and dictye (of v. Winiwarter), after which they all degenerate. In the definitive oocytes there is no evidence of synizesis nor of synapsis (conjugation of the chromosomes), but the chromatin network, very delicate at first, becomes heavier, and then becomes attenuated as the cell grows in size. The definitive ova develop after birth by a process of differentiation from the cells of the germinal epithelium. Stages were seen transitional between mesothelial cells and primary. These are fated to degenerate. The suggestion is repeated that this is a stage in degeneration in which the normal relations of nucleus and cytoplasm are disturbed. The fact that similar stages have been found in somatic cells militates against the attributing of any special genetic significance to this condition in the germ cells.—E. R. H.

158. (OVARY) Seniladad prematura y atrofia genital. (Premature senility and genital atrophy.) Turenne (A.) Revista Médica del Uruguay (Montevideo), 1917, **20**, 742.

Turenne reports a very interesting study of the pathogeny of some of the genital atrophies. He obtained in four cases a history of puerperal infection which was followed in a short time by amenorrhea, whiteness of the hair, senile appearance of the skin and loss of the teeth without caries. The patients were observed from two to three years after the puerperal infection. A characteristic genital atrophy developed. The uterus diminished in size,—in case of one 6-para having a length of but 6 cm.,—and the vagina and labia majora also showed atrophy. In one patient obesity preceded the genital atrophy and early senility appeared; the mammae, however, remained normal in appearance. G. P. G.

159. (OVARY) Sex Studies. X. The corpus luteum in the ovary of the domestic fowl. Pearl (R.), and Boring (A. M.), Am. Jour. Anat. (Phila.) 1918, **23**, 1.

Evidence is presented in this study which is believed sufficient to demonstrate that there is normally found in connection with the discharge or degeneration of the ovarian follicle in the domestic fowl a structure which is homologous to the corpus luteum of the mammalian ovary. The origin of this structure in the bird is plainly simply from the theca interna. The course of development of the bird's corpus luteum is an abbreviation of that in the mammal.—E. R. H.

160. (OVARY) Sex studies. XI. Hermaphrodite birds. Boring (A. M.) and Pearl (R.) Jour. Exp. Zool. (Phila.) 1918, Vol. 25.

This paper is a detailed study of the external characters, behavior, anatomy, and cytology of a series of hermaphroditic fowls and guinea-chicken hybrids. The more significant general results obtained are as follows: The eight hermaphroditic fowls studied were all basally females with ovaries in various stages of embryonic arrest of development or degeneration. Three of the lot were demonstrably changing from the female to the male condition in respect of the structure of the gonads, secondary characters, and behavior. The assumption of male behavior (treading) by an otherwise normal female has no demonstrable basis in changed structure of the gonad. The sex or degree of activity of the gonad has no direct causal relation to the development of comb, spurs, and wattles. Body shape and carriage have a general relation to the sex of the gonad. The interstitial cells have, in this material, no causal relation to the secondary sex characters. The amount of lutear cells or pigment is in precise correlation with the degree of external somatic femaleness exhibited by the individual.—E. R. H.

161. (OVARY) The formation and structure of the zona pellucida in the ovarian eggs of turtles. Thing (Alice) Am. Jour. Anat. (Phila.), Vol. 23.

The ovarian eggs of the various forms studied are surrounded by a single layer of prismatic epithelial cells, which are separated from each other at the surface by a special cement, the terminal bars. The zona pellucida is to be looked upon as a cuticular formation, taking origin in large part from these terminal bars. It varies in thickness from 1 to 22 micra,

depending on the stage, and early (3 micra) may be divided into an outer denser and thicker and an inner thinner, clearer, and striated layer. Later growth and differentiation occur mainly in the outer layer. The zona is made up of a homogeneous fundamental substance traversed by numerous fine canals, in which are contained filaments or prolongations of the epithelial cells outside, connecting these cells with the surface of the yolk beneath the zona. These prolongations vary in length with the thickness of the zona and end in knob-like enlargements on the yolk. The fundamental substance of the zona arises in part from a delicate secondary network within the primary network of the terminal bars which is apparently produced by the superficial cytoplasm of the cells and which gives rise at its surface to a cuticular substance similar to that derived from the terminal bars. From these networks are derived, as the thickness of the zona increases, the fundamental substance and its enclosed canals, thus presenting a structure well adapted to the conveyance of nutritive material from the maternal blood to the growing yolk.—E. R. H.

162. (OVARY) The winter cycle of egg-production. Goodale (H. D.) Anat. Rec. (Phila.) 1918, Vol. 14.

Of no direct endocrine interest.

163. (OVARY) Tubal and ovarian hemorrhage; its etiologic relation to pelvic hematocele and extra-uterine pregnancy. Bovee(J. W.) Proc. Am. Gyn. Soc., Jour. A. M. A. (Chgo.) 1918, **70,** 1975.

"Trauma plays a part in producing these hemorrhages. Hemorrhage from the fallopian tube may occur from general conditions that similarly affect othe rtissues. Venous stasis from circulatory disturbances or pressure from tumors may reasonably be included in a list of its causes. Ovarian hemorrhage may be confined within the ovary, constituting one or more hematomas, or it may take place into the peritoneal cavity, producing, if abundant, a hematocele. No other organ of the body is so frequently the seat of hemorrhage as is the ovary. Stromal hemorrhage is commonly preceded by infection of the ovary. In but few cases have correct diagnoses been made before operation or necropsy. As to treatment, in the milder forms of the condition rest and anodynes may meet all indications. In the severer forms the same rules apply as are employed in the treatment of ectopic pregnancy."

164. (PANCREAS) Pancreatic diabetes. Hardoy (P. J.) Revista Assoc. med. Argentina (Buenos Aires), 1917, **27,** 123.

A man 21 years of age with positive Wasserman, considerable glycosuria, marked polyuria and emaciation (20 kg. lost in 3 mos.) was considered to have pancreatic diabetes. Functional tests indicated that the external secretion of the pancreas was normal. The author believed that the condition was due to relative over-activity of the sympathetic nervous system, the vagus being depressed. Accordingly he administered pilocarpine and the glycosuria disappeared. Allowing the patient the use of carbohydrate caused a return of the glycosuria which again yielded to pilocarpine treatment.—B. A. H.

165. (PANCREAS) Sugar absorption and the pancreas. v. Korsky (K.) Ztschr. F. physiol. Chem., 1916, **98,** 37-48.

Experiments on dogs are described which indicate that when the blood is prevented from circulating through the organs of the body, including the pancreas, the introduction of a large quantity of dextrose solution into the intestine leads to an increase in the amount of dextrose in the blood; while, if the pancreas is left in the circulation, under otherwise normal conditions, a decrease in the amount of dextrose in the blood is observed. Chem. Abst. **12,** 497.

166. (PANCREAS) The site of formation of fibrinogen. Wohlgemuth (J.) Berlin, klin. Wchnschr. (Berlin), 1917, **54,** 87-90.

The influence of the pancreas on the liver is not limited to carbohydrate metabolism, but is also related to protein metabolism, one effect being the liberation of fibrinogen into the blood. Chem. Abst. **12,** 933.

167. (PANCREAS) Morphine hyperglycemia in dogs with experimental pancreatic deficiency. Auer (J.) and Kleiner (I. S.). Jour. Exp. Med. (N. Y.), 1918, **27,** 49.

The authors contend that any factor causing hyperglycemia will probably call forth a greater response in animals with a pancreatic deficiency than in normal animals. This conclusion was substantiated by injecting morphine, 2 mg per kilo body weight, into the subcutaneous tissue of dogs that had previously sustained partial removal of the pancreas. In these animals it was found that morphine produced a rise in the glycemia about four times greater than the same amount of mor

phine calls forth in normal dogs. Animals with pancreatic deficiency may be considered to be in a prediabetic state, hence, inasmuch as morphine causes hyperglycemia in these experimental animals, the inference is drawn that this test should be of value in detecting a weakened carbohydrate metabolism in the human subject. The data presented afford additional corroboration of the view that the responses of a normal and of a pathologically altered organism to the same drug in the same dosage may show very large quantitative differences.—H. W.

168. (PARATHYROID) Action of the serum of normal dogs and of those in tetany on the muscles of toads and frogs. Houssay (B. A.) Revista Assoc. Méd. Argentina (Buenos Aires), 1917, **27**, 641.

The muscles of the frog, Leptodactylus ocellatus, were not influenced by the serum of either normal or tetanic dogs. The muscles of some toads, Bufo marinus, submerged in the serum of a dog in tetany showed contractions, but these were produced also by the serum of normal dogs.—B. A. H.

169. (PARATHYROID) The present day therapeutics of spasmophilia. Cozzolino (O.) La Pediatra (Napoli) 1916, **24**, 292. Abstr. Brit. J. Chil. Dis. (Lond.) 1917, **14**, 233.

Parathyroid opotherapy is discussed and attention drawn to the probable divergence in therapeutic value of preparations from too old or too young animals as not containing sufficient quantity of the active principle. The author considers that opotherapy in spasmophilia may, in the future, tend toward a pluriglandular or at least a parathyroid-thymic opotherapy. He lays stress on the value of proper feeding and care of slight ailments which may favor the development of convulsive manifestations.—M. B. G.

170. (PINEAL) Calcification in the pineal gland. Boas (E. P.) and Scholz (T.). Arch. Int. Med. (Chgo.), 1918, **21**, 66.

Case report of extensive calcification of the pineal gland in an individual 74 years of age. No symptoms referable to a diseased condition of the pineal body were demonstrable during the period of observation. At necropsy (death caused by a strangulated sliding hernia) areas of softening were found in the brain involving the external capsule and island of Reil on the right side, primary contracted kidneys, cholelithiasis, and extreme arteriosclerosis and calcification of the coronary arter-

ies, with calfication of a large part of the myocardium of the left ventricle. The pineal gland showed slight enlargement and marked calcification.

Pineal calcification is now known to be a not unusual finding in roentgenograms of the skull. In the majority of cases this calcification is only an exaggeration of the deposits of brain sand normally found in the glands of adults. Inasmuch as calcification occurs normally in the course of involution of the pineal gland such changes are insignificant save in preadolescent individuals. Calcification of the gland occurring at the period when the gland is normally physiologically active may result in symptoms due to insufficiency of pineal secretion.—H. W.

171. (PITUITARY) Effect of tethelin on experimental tuberculosis. Corper (H. J.) J. Infect. Dis. (Chgo.), 1917, **21**, 269.

Tethelin, a substance precipitated from the anterior lobe of the ox pituitary, has been shown by Robertson to have a stimulating action on growth in mice and rats. Because of this action, Corper suggests that tethelin might be used in the indirect therapy of tuberculosis by stimulating the resistance of the host to tubercle bacilli. Guinea pigs were infected with virulent human tubercle bacilli and injected on alternate days subcutaneously with 25 mg. doses of tethelin for 18 days, before and during the infection. Such procedure had no appreciable effect on the progress of the tuberculosis or on the duration of life of these animals. Tethelin administered in 25 mg. doses daily to guinea pigs sensitized to tuberculosis by dead and living human tubercle bacilli had no appreciable effect on the development, recession or rupture of intracutaneous tubercles produced by dead human tubercle bacilli, nor on deep puncture wounds of the skin in these animals.—Chem. Abst.

172. (PITUITARY) The influence of pituitary extracts on the daily output of urine. Rees (M. H.). Am. Jour. Physiol. (Balt.), 1918, **45**, 471.

An attempt to ascertain "whether the subcutaneous injection of pituitary extract will cause any quantitive variation in the daily output of urine" and "whether such injection will in any way affect the quantity of urine excreted, and, if so, to find out if possible, the factor involved."

The methods of Motzfeldt were followed, except that the

observations extended over longer periods of time. The conclusions reached are:

1. Subcutaneous injections of pituitary extract do not alter quantitatively the daily output of urine in cats and rabbits, nor do they cause any marked variation in the specific gravity of the urine.

2. The subcutaneous injection of pituitary extracts causes a delay of seven to eight hours before the beginning of the diuresis which follows the ingestion of large amounts of water.

3. The delay in diuresis which is produced by subcutaneous injection of pituitary extract is due in part at least to a delayed absorption from the alimentary canal.

4. The subcutaneous injection of pituitary extract has no influence on the diuresis induced by the continuous intravenous injection of isotonic salt solution.—T. C. B.

173. PITUITRIN, its value in post-operative treatment. Davis (N.) and Owens (R.). New Orleans Med. and Surg. Jour., 1918, **70**, 712.

The authors present an enthusiastic account of their experience with pituitrin in 126 laparotomies. Although they regard it as of little use in obstetrical practice, they believe that it has an important place in surgery. They conclude: "That pituitrin is a valuable drug in stimulating the muscular coats of the intestine after abdominal section in non-septic cases. It is of decided assistance in preventing post-operative shock. It has very little if any effect upon cases complicated with septic peritonitis, but our results are inconclusive on account of the small number of cases. It stimulates the secretory section of the kidneys in cases of eclampsia. It materially reduces the amount of post-operative suffering."—R. G. H.

174. (PITUITRIN) The regulation of renal activity. V. Regulation of urea excretion by pituitrin. Addis (T.), Barnett (G. D.) and Shevky (A. E.) Am. Jour. Physiol. (Balt.) 1918, **46**, 52-62.

The subcutaneous injection of pituitrin in the rabbit is followed in all effective amounts by a decrease in the urea excreting activity of the kidney. The rate of urea excretion is slower than in animals not given pituitrin, although the blood urea concentration is higher.—L. G. K.

175. (PITUITRIN) The value of pituitary extract in incomplete abortion and placenta previa. Lipkis (A.) Northwest Med. (Seattle), 1918, **17**, 74.

Pituitary extract in 0.5 c.c. doses will do away with the curette or pack in most, if not all, cases of incomplete abortion. It controls hemorrhage, and the placenta usually comes away within three days. In some few cases it may take longer—6 or 7 days. As a rule the longer the pregnancy and the larger the placenta the less time it will take for the uterus to empty itself and the more likely the placenta will come away as one piece. The advantage of this treatment over the prevailing method of cureting or packing is that it is simple, and by avoiding local manipulations, lessens the danger of infection.

In one case the author succeeded in delivering a placenta previa marginalis with one-fourth c.c. doses of pituitary extract.—Author's Abstract.

176. REPRODUCTIVE GLANDS, internal secretion of. Steinach, Foges, and Lode, Ztschr. f. Sexualwissensch. (Leipzig), August, 1917.

It is stated that after castration the sexual disposition of young mammals may be reversed by implanting a testis into females, or an ovary into males. The reproductive hormones are regarded as antagonistic, and the erotising effect does not occur if castration has not been performed. The "Lancet" in an annotation from which this is taken maintains a cautious attitude in reference to these results.—Physiol. Abst.

177. (SECRETIN) A new plant secretin. Bickel (A.) Berl. klin. Wchnschr. (Berlin), 1917, 552-3; Eisenhardt (W.) Ibid., 553-4; Djenab (K.) Ibid., 24-5. (Physiol. Abst., 2, 605.)

Spinach contains a secretin which acts both on the stomach and the pancreas. In the fresh vegetable it is firmly united, but can be boiled out by water or liberated by hydrolysis with HCl. It resists this action, but is destroyed at 140°. It is an organic substance with an activity about equal to that of pilocarpine. Its action is shown better by intravenous injection than by administration by mouth. The relation of secretins and vitamines is discussed. Confirmatory experiments by Eisenhardt on dogs with Pavlov stomachs are recorded. The stimulating substance is the arginine-histidine fraction. Its relation to vitamines is also considered. Djenab determined that when injected into a femoral vein it lowers blood pressure and causes secretion from the pancreas. Injected into the mesenteric vein, the fall of pressure is less and does not last as long; there is no effect upon the pancreas. The conclusion is drawn that it is neutralized in its passage through the liver,

and to some extent, through the muscular tissues. The same effect is produced on the true pancreatic secretin; examination of the various levels of the intestinal mucosa shows that secretin is most abundantly obtained in the deeper layers of the duodenal lining. Chem. Abst. **12**, 1069.

178. (SECRETIN, II) Its influence on the number of white corpuscles in the circulating blood. Downs (A. W.) and Eddy (N. B.). Am. Jour. Physiol. (Balt.), 1918, **45**, 294.

It is possible to produce an increase in the number of white corpuscles per cubic millimeter of blood by the administration of secretin, even in small doses and by subcutaneous injection.

The most efficient dose is 1 cc. of secretin solution per kilogram of body weight.

It is suggested that the effects described are due to a direct stimulating action of secretin on both the bone marrow and the lymphatic tissues in general.—T. C. B.

179. (SPLEEN) The elimination of iron and its distribution in the liver and spleen in experimental anemia. Dubin (H.), Pearce (R. M.) Jour. Exp. Med. (N. Y.), 1918, **27**, 479.

No increased elimination of iron was observed in the feces of dogs showing an essentially chronic experimental anemia produced by infecting the animals with Trypanosoma equiperdum. The storage of iron in the liver and spleen was slightly increased in amount, but of the same general character as in transient experimental anemia. Splenectomy before and after infection influenced neither the elimination of iron in the feces nor its storage in the liver. Retardation of the course of the trypanosome infection likewise failed to affect iron storage. In the presence of a bile duct-ureter fistula the iron content of the mixture of urine and bile was not appreciably greater than that of normal urine alone. Therefore, the elimination of iron in the bile does not seem to be an important factor in the dog. However, when bile is excluded from the intestine an unusual storage of iron occurs in the spleen. No explanation of the latter condition is offered.—H. W.

180. (SPLEEN LIVER) Hematogenous icterus, hemoglobin and iron metabolism. Lepehne (G.) Beitr. z. path. Anat., 1917, **64**, 55-126. (Physiol. Abst., 2, 25.)

Clinical work on jaundice and experiments on animals show that there is an inter-relationship of liver and spleen in reference to hemoglobin and iron metabolism. After the spleen

is extirpated in rats and mice the Kupffer cells of the liver become active, and phagocytosis and accumulation of iron occur in that organ. Differences in that respect occur in different animals: the guinea pig, for example, does not show the same effect as that manifested in rats and mice.

Chem. Abst. **12**, 939.

181. SPLENOMEGALY, Familial, a clinical study. De Lange (C.) and Schippers (J. C.) Amer. J. Dis. Child. (Chgo.), 1918, **15**, 249.

The authors report the clinical history of seven children in one family, at least two of whom, in their opinion, presented the clinical picture of Gaucher's type of splenomegaly. Case 1. The first child in the family died at the age of two years of "hepatitis." Case 2. The second child, 11 years old, had enlargement of both spleen and liver; skin was slightly yellow tinted; death occurred suddenly after a serious hematemesis. Case 3. The third child died at the age of 17 days from an umbilical infection. Case 4. The fourth child looked healthy; his spleen was palpable beneath the costal margin. Case 5. The fifth child did not show any enlargement of either spleen or liver.

Case 6. The sixth child, a girl of 7½ years of age, had a distended abdomen. The spleen was felt one-half inch above the anterior superior spine; the right border was 2½ inches from the median line. The liver extended 3 inches below the costal margin. The Wassermann reaction was negative, as in the previous cases, and the Von Pirquet, positive. The others were negative except Case 4. The blood showed leucopenia with increase, however, in the number of mononuclear lymphocytes. There was no marked anemia. Splenectomy was performed.

Case 7. The seventh child, a girl, 5½ years old, showed a few pigmented spots on the abdomen, but no jaundice. The spleen extended 1 inch above the anterior iliac spine; the right border was 2½ inches from the navel. Splenic dullness was heard in the axillary line at the ninth rib. The liver was enlarged, the Wassermann reaction negative, and Von Pirquet, positive. Blood examination showed a leucopenia varying from 4200 to 8500, hemoglobin in very large amount, and a high count of erythrocytes. Splenectomy was done. The mother said that the enlargement of the liver and spleen was already noticed in this case at the age of two and in Case 6, at the age of four.

Examination of the father did not show any abnormalities; no enlargement of the spleen or liver. While his blood examination was practically normal on three tests, there was a con-

glycogen in the liver, the blood sugar being thereby mainstant relative lymphocytosis. The authors emphasize this latter point, although they do not venture to state that the disease in the children can be traced back to the father. Clinical and blood examinations of the mother, maternal and paternal grandmother and maternal grandfather were all negative.

After the operation the blood of both children showed an increase in leucocytes. The liver in one decreased somewhat in size and then remained stationary, while in the other, it increased slightly and then returned to the size preceding the operation. Both children were in good health a year after the operation.

Microscopic examinations did not show the accepted pathological picture of Gaucher's disease. The authors think, however, that they are dealing with a familiar progressive disease of the spleen which produces, sooner or later, an increasing cachexia and in the course of which a hemorrhagic diathesis occurs ante-mortem.—M. B. G.

182. SUGAR METABOLISM AND DIABETES. McGuigan (H.). Jour. Lab. and Clin. Med. (St. Louis), 1918, **3**, 219.

An interesting paper dealing with the history of diabetes and the various chemical tests used in the determination of sugar.—H. W.

183. (TESTES) Cases showing remote results of testicle implantation. Lydston (G. F.) Jour. A. M. A. (Chgo.) 1918, **70**, 907-8.

Two cases are described in which testes of boys 14-15 were implanted in the scrota of men lacking these organs. A marked development of virility followed. The author concludes that when technic and material are right and the recipient is properly selected, continuity of hormone production by the implanted gland for at least a prolonged period is certain and that permanent beneficial results are probable.—R. G. H.

184. (TESTIS) Chrondriosomes in the testicle cells of Fundulus. Duesberg (J.) Am. Jour. Anat. (Phila.) 1918, **23**, 133.

In the cells lining the proximal part of the excretory ducts in the testicle of Fundulus the chondriosomes are represented by long chondrioconts, whose disposition reminds one of the Heidenhain's or of the Pflüger's rods. In the latter part of the excretory ducts the chondriosomes are replaced by granules of pigment. The connective tissue of the testicle holds a num-

ber of cells with special characters (bacilli-shaped chondrioconts, secretion granules); these cells are probably interstitial cells. Chondriosomes are found in all generations of germ cells and transmitted during mitosis from one generation to the following one.—E. R. H.

185. **(TESTIS) The influence of excessive sexual activity of male rabbits. I. On the nature of the seminal discharge.** Lloyd-Jones (O.) and Hays (F. A.) Jour. Exp. Zool., (Phila.) 1918, Vol. 25.

Of no direct endocrine interest.

186. **(TESTIS) II. The influence of excessive sexual activity of male rabbits on the nature of their offspring.** Hays (F. A.) Jour. Exp. Zool. (Phila.) 1918, Vol. 25.

Of no direct endocrine interest.

187. **(TESTIS) The relations between the interstitial gland of the testicle, seminiferous tubules and secondary sexual characters.** Loeb (L.) Biol. Bull. (Woods Hole) 1918, Vol. 34.

The author found that a guinea pig with certain female secondary sex characters was an abnormal male. The testes were small, had not descended and were made up of interstitial cells, and typical tubules which lacked spermatogonia. The interstitial cells were abnormal containing vacuoles and eosinophilic bodies. The mammary gland was female in character.—E. R. H.

188. **THYMUS and dwarf growth.** Krabbe (K. H.) Ugeskrift. f. Laeger (Kobenhavn), 1917, **79,** 1329.

A case of pronounced dwarf growth is described and it is suggested that the thymus is responsible for the condition. There were no symptoms indicating abnormal functions of the thyroid, parathyroids, pituitary, suprarenals, ovaries or pancreas.—Physiol. Abst.

189. **(THYMUS) Extirpation of the thymus gland in Rana pipiens larvae.** Allen (B. M.)Anat. Rec. (Phila.) 1918, Vol. 14.

The thymus gland anlagen were removed at their very inception from 8 mm. to 9 mm. tadpoles. This was accomplished by cutting into each side of the head with a cataract

needle. Although the severity of the operation retarded development for a time, recovery was rapid and complete. Seven specimens were reared to the time of metamorphosis, attaining normal size and appearance. All died or were killed at this time. It is impossible from the material at hand to determine whether the high mortality at this time was due to the absence of the thymus gland or to other causes. It was in sharp contrast to the fate of the controls. Further experiments will be made upon this point next year. They appeared to be structurally normal in every regard. The characteristic features of metamorphosis occurred. A careful study of the thymus gland region of each specimen showed that the glands had in each case been successfully removed. Five out of the seven were males. Sexual differentiation was complete, and measurements showed the gonads to be altogether normal in size as compared with metamorphosed controls. A comparison of sections of the gonads of operated and control specimens showed those of both to be identical in structure and in the developmental stage reached by the germ cells.—E. R. H.

190. (THYMUS) Is the influence upon development, metamorphosis. and growth of thymus. when taken as food, due to a specific action of that gland? Uhlenhuth (E.) Jour. Exp. Zool. (Phila.) 1918, Vol. 25.

The differences in the rate of growth between thymus-fed and worm-fed larvae of Amblystoma opacum and A. punctatum are not the result of a specific growth-promoting influence of the thymus. but are due to the circumstance that animals which are better fed grow more rapidly. In order to make this point clear. quantitative feeding experiments were introduced in the study of the effect of the thymus. The meaning of the results regarding the effect of the thymus on development and metamorphosis will not become entirely clear before extensive experiments are available concerning the relation between size, rate of growth, differentiation, age, and metamorphosis in animals which have been fed on only one kind of food. When thymus-fed larvae of A. opacum and punctatum metamorphose, they are smaller than worm-fed animals at the time of metamorphosis. Larvae of A. opacum develop more rapidly when fed on thymus than do the controls; but only some thymus-fed individuals metamorphose earlier, while the development of others ceases (except development of the skin). when they reach the stage preceding metamorphosis. and either metamorphose only after a relatively long time or die as larvae after a certain period. Thymus-fed A. punctatum behave similarly. Two of these species, kept in low temperature, remained larvae

for about fifteen months, and died after they had commenced to metamorphose. Similar cases, however, are found even among worm-fed animals. It seems that the thymus does not interfere with those factors necessary for differentiation during the larval period; when metamorphosis begins, a new factor seems to become indispensable to further differentiation, and the thymus diet apparently often disturbs in some way the development of this factor. After a thymus-fed larva has once metamorphosed, it may live on exclusive thymus diet to at least eighteen months of age.—E. R. H.

191. (THYMUS) Klinische Bedentung der Thymusdrüse. (The clinical significance of the thymus.) von Haberer (H.) Arch. f. klin. Chirurgie (Berlin) 1917, **109**, 193.

In every case of partial thyreodectomy in Graves' disease it is necessary to look for the thymus and to enucleate it. The results of this combined operation are much better than when only a part of the thyroid is removed. There are classical cases of Graves' disease in which the thyroid is small, the thymus, however, being very large. In these cases complete recovery is observed after resection of the thymus.

The author operated on 40 cases in this way; he never observed a relapse. In young children the growth continued perfectly normally after removal of the thymus—J. K.

192. (THYMUS) Physiologie der Drüsen. Asher (L.) XXXIII. Eine neue Funktion des inneren Sekretes der Thymusdrüse. Müller (H.) Ztschr. f. Biol. (München), 1917, **67**, 489.

In frogs narcotised with urethane the triceps was fatigued by the method of Kornecker. In eight experiments Thyroglandol (La Roche) and in fifteen experiments a fresh watery extract of thymus was injected into the abdominal cavity and the effect on the height of the successive contractions was noted. The normal muscle fatigue curve descends gradually in a straight line. Provided fatigue were not too pronounced, both preparations caused its temporary disappearance in spite of continued stimulation, the height of the contractions (1) remaining stationary or (2) showing a slight increase; eventually the typical curve of fatigue reappeared. The action of thyroglandol was characterised by a latent period of twenty minutes, and was less marked than that of the fresh extract. Nucleoprotein, Ringer's solution and pituglandol, had no effect on the fatigue curve, and the author concludes that the beneficial action of thymus is specific. The physiological and patho-

logical significance of this new function of the internal secretion of the thymus is evident. Rabbit serum had a distinctly beneficial action on muscle fatigue, whereas plasma was inactive.—Physiol. Abst.

193. (THYMUS) Transplantation of the thymus in rabbits. Relation of the thymus to sexual maturity. Marine (D.) and Manley (O. T.). Jour. Lab. and Clin. Med. (St Louis), 1917, **3,** 48.

Transplants of thymus tissue in the subcutaneous tissues of the abdomen survive in sexually immature rabbits. Only auto-transplants persisted. The present experiments conform with the result of others and demonstrate that removal of the thymus hastens sexual maturity. Utilization of rabbits for breeding purposes hastens not only normal involution of the thymus but also the auto-transplants as well. This condition suggests that a specific nerve influence is not essential for these involutionary changes.—H. W.

194. (THYMUS) Report of nineteen cases of hyperphasia of the thymus gland, treated by the X-ray. Benjamin (J. E.) and Lange (S.) Arch. Ped. (N. Y.) 1918, **35,** 70.

The authors found that out of 225 cases of all sorts seen in their children's clinic, 19, or 8.47 per cent, showed undisputed evidences of enlarged thymus.

The chief complaint is nearly always a history of a cough in a child who does not show the prodromal symptoms of a cold but is apparently well. The cough is generally present at night and may be accompanied by a choking sensation.

The "threshold method of percussion" was used to outline the thymus. The child is placed on the mother's lap on his back. Percussion is begun well out in the chest, with such light strokes that when the ear is within a few inches of the area percussed only faintest possible resonance is heard. When sound disappears, dulness begins. Some observers outline the border of dullness by the tactile sense of resistance rather than sound. The outer borders are determined more easily than the lower boundary; the latter may be obtained by auscultatory percussion and is relatively less important. The writers found that the percussion outlines determined in this way correspond remarkably closely to the Roentgenogram. A clinical diagnosis of thymic enlargement is never absolutely positive without X-ray confirmation.

X-ray diagnosis is based upon an enlargement (usually lateral) of the thymus shadow, which normally rests upon and

is continuous with the heart shadow, which may, however, be confused with the shadow of congenital heart enlargement. In all cases where the diagnosis by the X-ray was doubtful, a therapeutic test of an X-ray exposure was given and found to be very reliable. Many symptomless and supposedly healthy children may show an apparently enlarged thymus upon the X-ray plate. An enlarged thymus in an apparently healthy child may be abnormal although its ill effects may not be manifest until some added strain be put upon the heart or respiratory organs or until the resisting powers of the child be called upon to overcome an acute infection.

Three treatments were the usual number given at intervals of one week, unless the urgency of the symptoms suggested more frequent applications, when a second dose was given in a day or two. In the average case the improvement was noted in 24 to 48 hours after the treatment.

The X-ray therapy in these cases was carried out as follows: A Coolidge tube backing up a 9½ inch spark was employed. The rays were filtered through 4 millimeters of aluminum and a piece of thick leather. The target skin distance was approximately nine inches. The routine exposure was 25 milliampere-minutes. In mild cases a single dose over the anterior surface of the chest proved sufficient. In more urgent cases 50 milliampere-minutes were administered at the first treatment, 25 anteriorly and 25 posteriorly. During the treatment the child was kept quiet by four sandbags, one placed across each arm and one across each leg. In order to get results it is essential that the treatments be comparatively heavy and that they be repeated at sufficiently short intervals.

The exposure varied from one-sixtieth to one-thirtieth of a second.—M. B. G.

195. (THYROID) Akuter Morbus Badedowi. (Acute Graves' disease.) Boir (C.) Klin. Monatsbl. f. Augenheilk (Berlin) 1917, **59**, No. 728.

Three cases are described, in which soldiers after a great fright, showed a classical picture of Graves' disease.—J. K.

196. (THYROID) Blutzuckerbestimmungen bei einem Fall von infantilen Myxödem. Nilsson (N.) Deutsche med. Wchnschr. (Berlin), 1917, **43**, 41.

Hypothyroidism is associated with a raising of the assimilation limit for glucose; hyperthyroidism with the opposite. In the present case (a boy aged seventeen) there was an increase of the blood sugar after giving either thyroid tablets or

adrenin. The effect on the blood picture is also described.—
Physiol. Abst.

197. (THYROID) Effects of the extirpation of the thyroid gland upon ossification in Rana pipiens. Terry (G. S.) Jour. Exp. Zool. (Phila.) 1918, Vol. 24.

Examination of the vertebral column of thyroidless and control tadpoles shows that the removal of the thyroid gland produces a marked retardation in the process of ossification which almost amounts to a cessation of the process. Up until the period when the hind legs begin to grow in length there is little difference in the process of ossification between the thyroidless and control specimens, but after this period the retardation becomes markedly noticeable in the thyroidless animals. In comparing the thyroidless and control specimens of the same age, calcification of the cartilage seems to take place at about the same time in both, but the erosion of calcified cartilage preliminary to ossification takes place very slowly in the thyroidless tadpoles. As a result of this, the vertebrae in older specimens appear more uniform than in the controls of the same age when studied from whole-mount preparations. The outline of the centrum is very regular and the calcification appears uniform in all specimens studied. There is a heavy deposition of calcium salts in the end of the rib, not present in control specimens. There is a complete absence of spinous processes upon the vertebrae of the largest thyroidless specimen (43 mm. body length from anterior tip of head to cloaca). Comparison of the hind legs of the control with much older thyroidless specimens with the same leg length shows that the removal of the thyroid gland has greatly retarded if not completely stopped both the processes of growth and ossification.—
E. R. H.

198. (THYROID) Effects of external temperature and certain drugs on thyroid activity. Mills (C. A.). Proc. Am. Physiol. Soc., Am. Jour. Physiol. (Balt.), 1918, **45**, 557.

199. (THYROID) Forma congestiva del hipotiroidismo. (Congestive form of hypothyroidism.) Mussio Fournier (J. C.) La Prensa Medica Argent. (Buenos Aires) 1918, **4**, 463.

A patient 53 years old had suffered from attacks of pulmonary congestion . . . anuria and hematuria and hemiplegia which had become ameliorated. The congestions had been treated repeatedly and the kidneys had twice been decapsu-

lated. As there were falling out of the hair, headache, insomnia. transitory edema of the limbs, etc., and the Wasserman reaction was negative and antiluetic treatment was always followed by symptoms of intoxication, it was decided to institute thyroid treatment. The results were gratifying; many of the symptoms gradually improved. Prof. Kocher introduced three thyroid grafts from a Basedow patient. An impovement of the symptoms, but also glycosuria, followed. Anginal attacks from which the patient had previously suffered reappeared, the arterial blood pressure reaching 220 mm. The author attributes these untoward results to the hyperthyroidism.—B. A. H.

200. (THYROID) Influence of thyroidin on standard metabolism. Krogh (M.) Ugeskrift for Laeger, 1916, No. **52.**

Determinations were made of the oxygen consumption by urethanized frogs before and after the administration of thyroidin; also with and without division of the nerve trunks for the four limbs. Thyroidin caused a much smaller rise in metabolism after the nerves were cut. It is accordingly provisionally concluded that thyroidin acts chiefly by increasing the tonus of striated muscle. Chem. Abst. **12,** 719.

201. (THYROID) Headache from thyroid deficiency. Giacobini (G.) Semana Médica (Bs. Aires.), 1918, **25,** 516.

A short paper, containing nothing new. G. P. G.

202. (THYROID) Sarcoma of the thyroid gland. Jorge (J. M.) and Arrillaga (F. C.) Revista Asoc. Méd. Argentina (Buenos Aires) (Dic.) 1917, **27,** 932.

A malignant sarcoma was observed in a woman 24 years of age. The case came to autopsy. Of the metastases present one especially worthy of interest had penetrated the veins of the neck and was prolonged to the interior of the heart.—B. A. H.

203. (THYROID) The acceleration of metamorphosis in frog larvae by thyroid feeding, and the effects upon the alimentary tract and sex glands. Swingle (W. W.) Jour. Exp. Zool. (Phila.) 1918, Vol. 24.

Very great acceleration of metamorphosis occurs in frog larvae when they are fed extract of thyroid gland. It is possible by judicious administration of thyroid to stimulate very immature tadpoles to complete metamorphosis, assuming all of

the adult characteristics except size. Examination of the gonads and germ cells reveals no observable changes, either gross or histological, from those of the control larvae of the same age and size; this despite the fact that from the standpoint of somatic development the thyroid-fed animals are months ahead of the controls.

The alimentary tract of tadpoles is a long, cylindrical, much-coiled structure, with little or no differentiation into stomach, small and large intestine. When the animals are placed upon thyroid diet the alimentary tract undergoes an extremely rapid differentiation to a well-marked stomach, small and large intestine. These changes occur within a few days. By thyroid feeding differentiation of the alimentary tract into its three characteristic divisions can be brought about in starved larvae in which all growth and development have ceased for months.

Drawings and photographs are given illustrating these points.—E. R. H.

204. (THYROID) The effect of the extirpation of the thyroid upon the thymus and the pituitary glands of Rana pipiens. Rogers (J. B.) Jour. Exp. Zool. (Phila.) 1918. Vol. 24.

The pituitary gland continues to develop when the thyroid gland is extirpated, the anterior lobe reaching a larger size in proportion to body length than it does in the pituitary gland in normal specimens. This is true in all stages up to young sexually mature normal frogs. In most cases the pituitary gland of the thyroidless tadpole is larger than that of the corresponding control without reference to body length. The pituitary gland is largest in proportion to body length in thyroidless tadpoles of the same age as young sexually mature frogs. The thymus glands continue to develop when the thyroid is extirpated. In metamorphosing controls they are much larger than those from thyroidless tadpoles of the same age. The thymus glands of the thyroidless tadpoles do not suffer degeneration like those of normal controls, but continue to grow; consequently those of thyroidless tadpoles do not migrate to the position in which the glands are found in adult frogs. The thymus glands of the thyroidless tadpoles grow to large size in later stages, but in early stages do not undergo the sudden increase in size that the controls do at metamorphosis.—E. R. H.

205. (THYROID) The effects of thyroid secretin on the excitability of the endings of the cardiac vagus. Levy (L.). Arch. Int. Med. (Chgo.), 1918, **21**, 263.

The author's experiments were designed to determine whether or not the secretion of the thyroid gland increases the responsiveness of the vagus nerve terminations to electrical stimulation. If it does, as certain investigators maintain, thyroid secretion must be regarded as having a sensitizing effect on true sympathetic as well as on parasympathetic (vagus) endings.

In cats pithed to the mid-thorax it was found that repeated stimulations of either vagus with a given strength of stimulus resulted in a uniform series of responses, both as to degree of depressor effect and duration of cardiac inhibition. After inducing secretory activity of the thyroid through faradic stimulations of the central end of the cut cervical sympathetic, even at a time when increased pressor responses to a given dose of adrenin gave evidence that there had been a pouring out of thyroid secretion, there was no significant alteration in the depressor effect or duration of cardiac inhibition following stimulation of the vagus nerves. Therefore, it appears evident that after the thyroid gland has liberated its secretion in sufficient quantity to sensitize the sympathetic structures acted upon by adrenin in raising arterial pressure, there is no demonstrable effect on the excitability of the endings of the cardiac vagus.—H. W.

206. (THYROID) The aetiology and treatment of exophthalmic goitre with special reference to the use of radium. Aikins (W. H. B.) Can. Pract. and Rev. (Toronto), 1916, **41**, 323.

A review of the etiology of exophthalmic goitre followed by a brief account of the various forms of treatment.

A brief summary is given of the treatment by medicaments, organotherapy, and Roentgen rays, and hydro-therapy, but many cases do not respond to any of these. Seven cases are discussed in which radium treatment, usually combined with the administration of hydrobromate of quinine and ergotin and the application of ice-bags to the praecordia was very effective. In all cases a very great improvement or a complete cure was recorded.—L. G. K.

207. (THYROID) The fate of the ultimobranchial bodies in the pig (Sus scrofa). Badertscher (J. A.) Am. Jour. Anat. (Phila.), 1918, Vol. 22.

The ultimobranchial bodies in the pig participate in the formation of thyroid follicles. The portion of the gland in full term embryos that is derived from these structures is small in

comparison to the part derived from the median thyroid anlage. Colloid first appears in the follicles of the thyroid gland in embryos 75 m.m. long. Colloid first appears in the follicles of the ultimobranchial bodies in embryos 125 m.m. long.

The cephalo-caudal extent of the ultimobranchial bodies is equal to or nearly equal to that of the thyroid gland in embryos up to about 33 mm. long. In stages from about 50 mm. length to full term they usually lie in the posterior half of the thyroid gland, but may be found in the middle third or in the middle two-fourths of the gland. In the majority of late stages they are entirely imbedded. The ultimobranchial bodies in a thyroid gland may vary in size, in shape, in the degree of their transformation, and in their location in the lateral halves of the thyroid gland.

The developmental stages in which the ultimobranchial bodies can no longer be recognized structurally from the median thyroid anlage vary greatly. The transformation of their greater part may take place as early as in a 35 mm. embryo, but in the majority of stages examined it takes place in later stages. Even in full term embryos an entire ultimobranchial body may not be completely transformed.—E. R. H.

208. (THYROID) The influence of large doses of thyroid extract on the total metabolism and heart in a case of heart block. Aub (J. C.) and Stern (N. S.). Arch. Int. Med. (Chgo.), 1918, **21**, 130.

A case report of a woman 24 years of age showing auriculoventricular dissociation together with a systolic murmur and slow heart. The thyroid gland was not palpable. Thyroid extract was administered in increasing doses over a period of four months during which time the patient ingested a total of over 2,000 grains. During the last month the doses amounted to 28 grains per day. The basal metabolism was increased 47 per cent above normal and a rapid auricular rate, 120 per minute, followed the administration of the large doses of extract. Within 12 days after withdrawal of the extract the basal metabolism dropped to normal and within 19 days the auricular rate dropped to 71, which rate was thereafter maintained. The administration of thyroid extract had apparently no effect on the respiratory quotient or the blood sugar. Because of the increase in auricular rate without alterations in the ventricular rate it is suggested that thyroid extract does not increase the heart beat by direct action on the muscles, but through nervous elements.—H. W.

209. (THYROID) The influence of the thyroid of anastomosis of the phrenic and cervical sympathetic nerves. Marine (D.), Rogoff (J. M.) and Stewart (G. N.). Am. Jour. Physiol. (Balt.), 1918, **45**, 268.

A repetition of the experiments of Cannon, Binger and Fitz. In none of the animals were there any symptoms of Graves' disease. No respiratory hippus, and no exophthalmos. No histological difference between the two sides of the thyroid. No study of the metabolism seems to have been made.—T. C. B.

210. (THYROID) The isolation and identification of the thyroid hormone, etc. Kendall (E. C.). Proc. of Am. Physiol. Soc., Am. Jour. Physiol. (Balt.), 1918, **45**, 540.

The iodin-containing compound of the thyroid has the empirical formula $C_{11}\ H_{10}\ O_3\ N\ I_3$ and is shown to be tri-hydro, triiodo oxy-indol proprionic acid. Physiological testing has shown that this substance will relieve all the symptoms of cretinism and myxedema to the same extent as desiccated thyroid.

(It is assumed that a full report will appear later.)—T. C. B.

211. (THYROID) The physiological action of the thyroid secretion and a method for its demonstration. Asher (L.) Deutsche med. Wchnschr. (Berlin), 1916, **42**, 1028.

By stimulating the nerves of the thyroid, it is shown that certain biological reactions are obtained which occur when thyroid preparations are given. For practical purposes the most useful reaction to demonstrate the thyroid secretion is the strengthening of the adrenin action with the Laewen-Trendelenburg preparation. By this method it is possible to demonstrate the presence of an increased thyroid secretion in the blood of cases with Basedow's disease. It can further be shown that by feeding rats with thyroid tablets an increased formation of thyroid secretion occurs. The most important biological reaction is obtained not only by thyroid gland extract but also by the protein and iodine free "thyreo-glandol" prepared by Hoffman-LaRoche, Basel. It produces the same action on metabolism as the whole gland.—Chem. Abst.

212. (THYROID) The prevention of simple goiter in man. Marine (D.) and Kimball (O. P.). Jour. Lab. and Clin. Med. (St. Louis), 1917, **3**, 40.

From a complete census of the condition of the thyroid gland in 3,872 girls from the 5th to the 12th grades of the school population of a large community in the Great Lakes goiter district, it was found that 1,688, or 43.59 per cent, had normal thyroids; 2,184, or 56.41 per cent, had enlarged thyroids; and 594, or 13.4 per cent, had well defined, persistent thyroglossal stalks.

From the results of experimental work and general conclusions a method of prophylaxis has been developed and put into practice. This consists of the administration of small doses of the iodides.—H. W.

213. (THYROID) The relation of normal thyroid-gland development to bodily growth and differentiation in Rana, Bufo, and Amblystoma. Allen (B. M.) Anat. Rec. (Phila.) 1918, Vol. 14.

In Amblystoma both fore and hind limbs begin to grow before any colloid is formed in the thyroid gland. In Bufo it appears almost immediately after limbs have begun to grow, while in Rana pipiens it appears practically simultaneously with anlage of the hind limbs.

In all three forms there is a rapid growth of the gland and this corresponds closely with limb development. In all three forms the thyroid gland is well developed and contains a large amount of colloid long before metamorphosis is completed.

In axolotls of 140-160 mm. length the thyroid gland was found to be approximately of equal size and structurally similar to that of adult Amblystoma tigrinum. Colloid was present in large amount in both, but the axolotls were not well enough preserved to enable one to judge of its density.

Although the thyroid gland of Bufo is actually smaller at metamorphosis than that of Rana or Amblystoma its proportion to body size is greater than in either Amblystoma or Rana. This is probably correlated with the shortness of its larval life and the greater rapidity of its metamorphosis.

There is a clear correspondence between the normal development of the thyroid gland and normal progress toward metamophosis, although limb development may be partly independent of it.—E. R. H.

214. (THYROID) The relation of the thyroid gland to regeneration in Rana pipiens. Allen (B. M.) Anat. Rec. (Phila.) 1918. Vol. 14.

These experiments involved three classes of tadpoles: 1. Tadpoles from which the thyroid gland had been extirpated

—absence of thyroid secretion. 2. Normal control tadpoles. 3. Tadpoles to which thyroid extracts were fed—excess of thyroid materials.

In each case approximately the terminal half of the tail was removed. Regeneration proceeded normally in quantity and in quality in all three groups. There was a certain amount of individual variation in the degree of regeneration, dependent upon the amount of material removed, the age, and upon individual factors, but the range in amount of regeneration was proportional to that in corresponding controls, in spite of the total length from 16.7 mm. to 58 mm. Class 3 was composed of tadpoles of intermediate size, ranging from 32.8 mm. to 45.1 mm. The amount of regeneration in this group was nearly proprotional to that in corresponding controls, in spite of the fact that the thyroid feeding had caused a marked shrinkage in body length and had caused one-half of the specimens to develop to the stage where one or both of the fore limbs had broken through the skin. We conclude from these experiments that the thyroid gland does not influence the process of regeneration.—E. R. H.

215. (THYROID) The results of thyroid removal in the larvae of Rana pipiens. Allen (B. M.) Jour. Exp. Zool. (Phila.) 1918, Vol. 24.

Removal of the thyroid gland anlage was accomplished when the tadpoles were from 6 to 7 mm. in length. Development proceeded normally until the hind limb buds appeared. From that time the tadpoles underwent structural development very slowly, but continued to increase in size until they attained a length of trunk of from 30 to 43 mm. measured from the anterior tip of the body to the cloaca. The hind legs reached a length of 5 mm. The fore limbs did not break through the skin. The controls underwent metamorphosis normally while kept under identical conditions. The brains of the thyroidless tadpoles remained approximately in the structural form found in normal tadpoles in a corresponding stage of development. In the length of the intestine, the character of the mouth, the persistence of the gills and in all other somatic features studied, the tadpoles retained the structural characteristics that had been attained at the time when metamorphosis was arrested.

The gonads behaved in sharp contrast to the soma in that they continued in the normal course of development to a condition far beyond that found at metamorphosis and comparable to that of normal young frogs killed at the same time (February following the operation). This was true of both ovary

and testis as regards form, structural development and relative size. In the thyroidless tadpoles ripe spermatozoa developed in large numbers and oocytes grew to twice the size found in young frogs at the time of metamorphosis.—E. R. H.

216. (THYROID) The thyroid gland and the oxidative ferments. Goldenberg (L.) La Semana Méd. (Buenos Aires), 1917, No. 50.

Thyroid extract added to iodin decolorized by zinc in an alkaline medium restored its reddish color. Sodium citrate prevented the reaction.—B. A. H.

217. (THYROID) Tratamiento del bocio exoftalmico por inyecciones de agua hirviendo. (Treatment of exophthalmic goitre by injections of boiling water.) Olivieri (E. M.), Ronchi (P.) Ceballos (A.) and Bacigalupo (G.) Soc. Med. Argent., 1917, (June 29).

Olivieri and Ronchi presented four cases subjectively and objectively improved by the treatment. They had less tachycardia, increase in weight (2 to 13 and 4.5 to 6 kg.) and diarrhea and vomiting ceased. Ceballos and Bacigalupo reported six cases, some of which improved gradually and some rapidly with no treatment other than the boiling water injections.—B. A. H.

218. (THYROID) Un caso de acondroplasis con antecedentes familiares de hipotiroidismo. (A case of achrondoplasia with family history of hypothyroidism.) Mussio (F.) Rev. Méd. Uruguay (Montevideo), 1917, **20**, 768.

Describes the case of a boy 15 years old, three of whose uncles had shown symptoms of hypothyroidism. The boy early developed signs of sexual maturity, including hirsuitism, adult genitalia and deep voice. Mussio thinks that the case is one of hypergenitalism associated with thyroid-pituitary insufficiency. G. P. G.

219. (THYROID AND THYMUS) Pharyngeal derivatives of amblystoma. Baldwin (F. M.) Jour. Morph. (Phila.) 1918, Vol. 30.

This paper deals with the morphogenesis of the thyroid and thymus glands, and postbranchial and epithelial bodies of Amblystoma, beginning with larvae 5 m.m. long, and including stages in a metamorphosis and adult. The thyreoid gland

arises as a solid outgrowth from the pharyngeal floor and breaks up into scattered cells, which, by mitotic division, give rise to the thyreoid follicles, in which colloid appears in late larvae. There is no evidence of the formation of accessory thyroids. Venous twigs form a rete mirabile around the follicles, but the jugular vein does not participate in this. There is no thyroid artery. The thymus gland arises from five pairs of anlagen, derived from the dorsal margins of the corresponding gill pouches. The anterior two degenerate, the other three form the definitive organ. There are no ectodermal contributions to the gland. The adult gland is three-lobed and is innervated by the ninth and tenth nerves. The postbranchial body arises from a thickening of the pharyngeal floor behind the last gill pouch. In all cases, with one exception, it was asymmetrical. In the adult it lies medial to the additus laryngeus muscle. It never contains colloid. The carotid gland has no connection with cells of the pharyngeal wall or those of the degenerating gill pouches. At the time of metamorphosis two pairs of epithelial bodies arise from the ventral parts of the last two gill pouches. In the adult they lie just below the thymus and are supplied with blood from the second afferent and external carotid arteries and are innervated by the vagus. They are the homologues of the parathyroids of the mammals.—E. R. H.

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